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## RECENT ADVANCES IN SERODIAGNOSTIC TESTS FOR SYPHILIS *


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This year marks the fiftieth anniversary of the discovery by Wassermann and his associates [1] that the application of the phenomenon of complement fixation could be used in the laboratory diagnosis of syphilis. Through the years, great advances and changes in the original technic have taken place and newer methods and tests have been developed. A brief review of the immunology of syphilis and some of the significant changes that have been made in the older tests using lipoidal antigen will contribute to a better understanding of the newer tests using specific treponemal antigens.

Wassermann employed an aqueous extract of syphilitic fetal liver as antigen in his original test believing that a specific antigenic component was contained in it. Soon thereafter, it was found that any normal mammalian tissue could be used in preparation of antigen and that an alcoholic extract was far more sensitive than an aqueous one. It was also discovered that the addition of cholesterol further enhanced the sensitivity of the test. It became evident that the Wassermann reaction was not a specific antigen-antibody reaction.

The term reagin, "because it reacts", was arbitrarily assigned to the active substance present in syphilitic serum and spinal fluid that reacts with lipoidal antigen. Thus far, neither the exact chemical composition nor immunologic properties of reagin have been determined. It has been classified as an antibody because, like antibodies in general, it reacts, is always associated with the gamma globulin fraction of serum and has a molecular weight similar to that of antibodies.

The substance responsible for the reactivity of the alcoholic tissue extracts was isolated from beef heart in 1941 by Pangborn.[2] This substance called cardiolipin, was found to be a non-nitrogenous phospholipid. Subsequent publication of the method of isolation and purification [3] led to the beginning of a new era in the standard serological tests for syphilis hereafter referred to as STS. Cardiolipin alone is feebly antigenic but with purified lecithin and cholesterol in proper proportions produces satisfactory antigens for complement fixation and flocculation tests.

The cardiolipin antigens have several distinct advantages over the cruder lipoidal antigens. Because they are reproducible, they allow for more uniform results; the sensitivity level is equal to or slightly higher than that of tests using lipoidal antigens, and cardiolipin tests are definitely more specific, as shown by comparative

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studies and evaluation surveys.

With the exception of Kahn, the authors of the Kline,[4] Kolmer,[5] Hinton[6] and Mazzini[7] standard STS have gradually modified the techniques of their tests to use cardiolipin antigen. Furthermore, new tests have been described, several of which are being used routinely by many laboratories in the United States and other countries. It is interesting to note that one of these, the VDRL Slide Test,[8] as shown by the report of the 1955 National Evaluation Survey, is used routinely by 41 state laboratories, experimentally by 2 and by official laboratories in Hawaii, Alaska, and Puerto Rico. It is also used by many hospital and private laboratories. For those who prefer a tube method, the VDRL tube test, using the same basic antigen gives equally good results. The tube test is also applicable for use with spinal fluids[10] which is of great advantage in laboratories which do not have facilities for performing complement fixation test.

Another test which is worthy of mention is the APHA Reference Microflocculation Test.[11] This was developed by a subcommittee of the American Public Health Association appointed to develop a microflocculation test for syphilis to be used as a reference test in setting the level of reactivity, thereby standardizing the serology of syphilis. A preliminary study by us[12] of a comparison of this test with other STS on a limited number of specimens showed the reactivity level to be slightly higher than that of the Kolmer complement fixation, VDRL and Kahn tests.

The cardiolipin tests are not sensitive enough to detect reagin in all stages of syphilitic infection, but they are generally considered satisfactory and of great help to the physician in the detection, treatment and control of syphilis. However, because of the large number of nonspecific reactions given by them in nonsyphilitic infections and presumably normal individuals their diagnostic significance has been questioned.

The detection and recognition of nonspecific reactions, referred to as "false-positive reaction" were known to the early workers, but since blood tests usually were made on persons who showed clinical or presumptive evidence of syphilis, these reactions were considered a rarity. With the institution of the so-called mass blood testing programs, such reactions assumed major importance. In mass testing programs thousands of persons with no history or clinical evidence of syphilis were found to be seropositive by one or more of the STS.

Physicians were often in a dilemma to decide if the positive reaction was due to syphilis or if it was produced by other conditions. Many patients on the results obtained by one or more of the STS were erroneously labelled syphilitic. They suffered untold embarrassment because of the social stigma attached to the disease; were denied employment, marriage license, entrance into armed services; were rejected as blood donors; given unnecessary treatment, and suffered considerable financial loss.

Detailed studies of the false-positive phenomenon have been made by many workers and much valuable information has been accumulated. Reaction with STS in patients with no clinical evidence of syphilis is now generally believed to be due to latent syphilis, either acquired or congenital, or what is now termed biologic false-positive reaction hereafter referred to as BFP.

Moore and Mohr[13] have divided the BFP reactions into two categories (1) "acute" and (2) "chronic" and have listed (Tables 1 and 2) some of the diseases and conditions known to give these reactions.

As noted, the acute BFP reactions are those which occur during or shortly after a large number of bacterial, spirochetal, plasmodial, rickettsial, protozoal, and viral infections. In this type, the amount of reagin in the blood of the patient is usually present in small amounts, is fluctuating, and disappears rapidly.

Chronic BFP reactions, on the other hand, are marked by the usual absence of a known precipitating factor and by the fact that reagin remains in the blood over

TABLE 1
ACUTE BIOLOGICALLY FALSE POSITIVE REACTIONS IN VARIOUS NONSYPHILITIC CONDITIONS
INFECTIONS

| DISEASE | Approximate Incidence of BFP Reactions % |
|---|---|
| **Bacterial** | |
| Leprosy | 60 |
| Tuberculosis, advanced | 3–5 |
| Pneumonia, pneumococcal | 2–5 |
| Subacute bacterial endocarditis | 5 |
| Chancroid | 5 |
| Scarlatina | 5 |
| **Spirochetal** | |
| Leptospirosis | 10 |
| Relapsing fever | 30 |
| Rat-bite fever | 20 |
| **Plasmodial** | |
| Malaria | 100 |
| **Rickettsial** | |
| Typhus | 20 |
| **Protozoal** | |
| Trypanosomiasis | 10 |
| **Viral** | |
| Vaccinia | 20 |
| Pneumonia, "atypical" | 20 |
| Measles | 5 |
| Chickenpox | 5 |
| Lymphogranuloma venereum | 20 |
| Infectious hepatitis | 10 |
| Infectious mononucleosis | 20 |
| Common cold | ? low |

TABLE 2
CHRONIC BIOLOGICALLY FALSE POSITIVE REACTIONS IN NONINFECTIOUS DISEASES OR CONDITIONS

| | Approximate Incidence of BFP Reactions % |
|---|---|
| Lupus erythematosus (disseminated or discoid) | 20 |
| Rheumatoid arthritis | 5 |
| Blood loss, repeated (as in multiple donations for transfusions) | ? low |
| Pregnancy | ? low |

a period of many months or years, perhaps even a lifetime. Moore and Mohr [13] in a preliminary study of the background of patients giving chronic BFP reactions are convinced that the BFP reaction is not as innocuous as formerly believed and that many of the collagen diseases such as disseminated lupus erythematosus, periarteritis nodosa, rheumatoid arthritis, rheumatic fever, and sarcoid give chronic BFP reactions. Moore and Lutz [14] in a later study of the clinical etiological background in 148 chronic BFP reactors were able to verify a diagnosis of systemic lupus erythematosus in 10 of the patients, while 7 of the group developed rheumatoid arthritis and 45 showed probable collagen vascular diseases.

The need of a specific test to separate syphilitic infection from chronic BFP was apparent. Many tests, including the so-called "verification tests" were claimed to be capable of differentiating positive results in syphilis from those produced by BFP reactors. All of these tests used lipoidal antigens and depended on the nonspecific antibody reagin. They proved to be no more specific than the STS. It was obvious that a specific test was not possible until the development of an in vitro method of cultivating virulent *Treponema pallidum*.

In 1948, Nelson [15] was successful in developing a basal medium for isolating and sustaining the growth of the virulent Nichols strain of *Treponema pallidum* for a period of six to eight days. Such a medium led to the development by Nelson and Mayer [16] of the "treponemal immobilization or TPI test". This test procedure proved capable of detecting the specific antibody in sera from syphilitic animals and human beings. In addition, the antibody was proved to be distinct from reagin and, except for the related treponematoses (yaws, pinta, and bejel), was a specific test for detection of syphilitic infection.

The work of Nelson and Mayer was enthusiastically received both in the United States and abroad and soon many TPI laboratories were set up and studies were initiated to investigate the clinical significance of the test.

The technic of the test as described by the authors consisted in incubating a test mixture of treponemal suspensions, complement and patient's sera under anaerobic conditions at 37°C for fifteen to eighteen hours. The mixture was then examined by

darkfield microscopy. In mixtures containing syphilitic serum, the treponemes were immobilized while in normal serum the organism remained motile.

Using the author's technic, many were unable to obtain consistent results. One of the main difficulties encountered was the poor survival of the treponemes in the basal medium during the duration of the test. To overcome this difficulty several modifications[17-21] of the original basal medium have been made and adopted by different workers. Reproducibility of reactions[22, 23] and other factors were also found to give inconclusive results.

In spite of many obstacles encountered with the TPI test, many laboratories are now performing it satisfactorily. From numerous reports in the literature, the test has now been applied to thousands of serums and spinal fluids from both normal and syphilitic patients. Zellman[24] has made a study of the specificity of the TPI test and has used the results obtained by him and other workers in the United States, France, Scandinavia, and Germany to compile a detailed statistical analysis of the TPI test in nonsyphilitic and syphilitic infections. (Tables 3, 4, and 5)

Table 3 gives an analysis of the TPI test on 1,397 nonsyphilitic individuals. The treponemal immobilizing antibody is not present in the serum of normal individuals and only present in 0.3 per cent of individuals in nontreponemal diseases. This small percentage may be due to technical error. The high specificity of the test makes it an ideal test for the differentiation of syphilitic infection from BFP reactions.

Table 4 gives an analysis of the TPI test on 2,280 syphilitic individuals. The TPI antibody appears in the serum soon after infection and remains elevated during untreated syphilis. It does not tend to disappear spontaneously like reagin. For this reason, the test is valuable in making a diagnosis of latent syphilis, acquired or congenital, especially in cases when the reagin tests are negative.

If treatment is instituted early, the treponemal antibody disappears, but at a slower rate than reagin, making the reagin tests more satisfactory as a treatment control. If treatment is delayed beyond the secondary stage, the treponema antibody tends to remain in the blood indefinitely.

The inherent technical difficulties in the

TABLE 3
THE TREPONEMAL IMMOBILIZATION TEST IN NONSYPHILITIC INDIVIDUALS

| Diagnostic Category | Number of Cases | TPI Results | | | |
|---|---|---|---|---|---|
| | | Positive | Doubtful | Negative | |
| Normal | 389 | 0 | 0 | 389 | 100% |
| Diseases other than syphilis | 615 | 1 | 1 | 613 | 99.7% |
| Nonsyphilitic * | 393 | 2 | 0 | 391 | 99.5% |
| Total Nonsyphilitic | 1397 | 3 | 1 | 1393 | 99.8% |

* not classified.

TABLE 4
THE TREPONEMAL IMMOBILIZATION TEST IN SYPHILITIC INDIVIDUALS

| Diagnostic Category of Syphilis | Number of Cases | TPI Results | | | |
|---|---|---|---|---|---|
| | | Positive | Doubtful | Negative | |
| Untreated primary | 174 | 97 | 16 | 61 | 64.9% |
| Untreated secondary | 591 | 553 | 15 | 23 | 96.0% |
| Untreated symptomatic | 288 | 228 | 0 | 0 | 100% |
| Untreated congenital | 74 | 68 | 1 | 5 | 93.0% |
| Treated primary | 254 | 109 | 9 | 136 | 51.9% |
| Treated secondary | 257 | 146 | 12 | 99 | 61.4% |
| Treated late symptomatic | 574 | 549 | 3 | 22 | 96.1% |
| Treated congenital | 128 | 111 | 3 | 14 | 89.0% |
| Total syphilitics | 2280 | 1861 | 59 | 360 | 84.2% |

TPI test soon gave impetus to search for a simpler test procedure in detecting the specific antibody. Nelson,[25] in 1952, was able to demonstrate the in vitro phagocytosis of *Treponema pallidum*. This led to the recognition of a specific reaction[26] between normal human erythrocytes and treponemes sensitized by antibody from syphilitic serum. The term immune adherence or TPIA was given to the phenomenon and a test procedure for its recognition developed.

Briefly, the technic of the test, as described by Nelson, consists in mixing a heat-killed suspension of treponemes with patient's serum. Human complement and a 50 per cent suspension of washed human blood cells are added to the mixture and after thirty minutes at 37°C this mixture is centrifuged and the treponemes in the supernatant counted by darkfield microscopy. Serums from syphilitic patients show a disappearance of treponemes in the supernatant, while no such disappearance occurs in nonsyphilitic serum.

The immune adherence (TPIA) test seems to have several distinct advantages over the TPI test. The test procedure is simpler and more rapid. An important feature is that heat-killed *Treponema pallida* are used as antigen. Antigens may now be purchased in limited amounts commercially.

Early attempts towards the development of a satisfactory agglutination test (TPA) for detecting agglutinins in response to *Treponema pallidum* were beset with difficulties in the preparation of antigen. The chief obstacle with early antigens was a tendency towards spontaneous agglutination of the organism. Several workers[27-30] have been successful in overcoming this difficulty by various methods and have described what they believe to be quite simple, sensitive, and specific agglutination tests. However, McLeod and Stokes[31] found that the TPA test detects at least two antibodies, one of which is reagin. They feel that "the agglutination technic as a specific diagnostic test for syphilis must await the preparation of more specific antigens".

Portnoy and Magnuson[32] have recently described the preparation of an antigen from virulent *Treponema pallidum* and its satisfactory use in a complement fixation test (TPCF). In the preparation of the antigen, the serologically active substance was extracted from *Treponema pallidum* by the use of desoxycholate solution. The Kolmer technique, using one-fifth volume to conserve antigen, was used in the test procedure.

A preliminary study of the incidence of TPCF antibody in human sera from 169 syphilitic cases and 383 sera from a general hospital admission indicate that the test shows a close correlation to TPI, suggesting a high specificity. The TPCF appears to be more sensitive than TPI in detecting primary and secondary syphilis but less sensitive than TPI in latent and late syphilis.

TPCF antigen in limited quantities is available from one biological house and another announces it is in the process of manufacture. Since many laboratories have facilities and personnel trained in complement fixation technique, it is anticipated that further evaluation will be made of the reliability and usefulness of the test as a diagnostic procedure. However, because of the limited supply and high cost of the antigen at the present time, it will only be used on selected and special cases.

TPCF antigen in limited amount has recently been obtained by us and 46 TPCF tests run in our laboratory, the results of which will be shown in the following tables.

Table 5 shows the results of TPCF and STS on 14 sera taken from hospital patients who gave no history or clinical evidence of syphilis. In this group of nonsyphilitic cases, the TPCF and VDRL slide test were nonreactive in all 14 cases, while the Kolmer complement fixation test showed reactive reactions in 2 of the 14 cases.

Table 6 shows results of tests in a group of 15 nonsyphilitic individuals suffering from various types of infections known to give acute BFP reactions. Of the group, 14 gave negative and one anticomplementary results with the TPCF, 4 were reactive in both the Kolmer complement fixa-

TABLE 5
RESULTS OF STS AND TPCF TESTS
(ROUTINE NONSYPHILITIC HOSPITAL CASES)

| Serum Number | Kolmer CF | VDRL Titer | TPCF | Clinical Diagnosis Age | Color | Sex | Cases |
|---|---|---|---|---|---|---|---|
| 12MX | — | — | — | 17 | W | F | Surg. |
| 13M | — | — | — | 27 | W | F | OB |
| 14M | — | — | — | 25 | W | F | OB |
| 15M | — | — | — | 20 | W | F | OB |
| 16M | — | — | — | 46 | W | M | Med. |
| 17M | — | — | — | 74 | W | M | Heart |
| 18M | — | — | — | 36 | W | F | Med. |
| 19M | — | — | — | 23 | W | F | OB |
| 20M | — | — | — | 24 | W | F | OB |
| 21M | — | — | — | 21 | W | F | OB |
| 22M | — | — | — | 32 | W | M | Surg. |
| 23MX[2] | R(4) | — | — | 28 | W | F | Surg. |
| 24M | — | — | — | 52 | W | M | Heart |
| 26MX[2] | R(1) | — | — | 57 | W | F | Surg. |

TABLE 6
RESULTS OF STS AND TPCF TESTS
(DISEASES OTHER THAN SYPHILIS)

| Serum Number | STS Kolmer CF | VDRL Titer | TPCF | Clinical Diagnosis Age | Color | Sex | Case |
|---|---|---|---|---|---|---|---|
| 9821 | Anti | — | Anti | 30 | C | M | Arrested leprosy |
| 9822 | — | — | — | 61 | C | M | Lepromatous leprosy |
| 1H | R(4) | 4 | — | 28 | W | M | Infectious mononucleosis |
| 10071 | — | — | — | 36 | C | F | Inactive T.B.—Preg. |
| 10072 | — | — | — | 28 | C | M | Arrested T.B. |
| 10073 | R(4) | 4 | — | 37 | C | F | Active T.B. |
| 10074 | — | — | — | 28 | C | F | Active T.B. |
| 10075 | — | — | — | 34 | C | F | Active T.B. |
| 10076 | — | — | — | 38 | C | M | Arrested T.B. |
| 73938 | — | — | — | 16 | W | M | Mumps encephalitis C.F. test—Pos. |
| 9439 | — | — | — | 39 | W | F ) | 1st. & 2nd. spec. |
| 9438 | — | — | — | 39 | W | F ) | suspected Psittacosis |
| 19021 | R(3) | WR | — | 28 | W | M | Clinically RMSF C.F. (RMSF) pos. 1-1028 |
| 19034 | R(3) | — | — | 26 | W | M | Clinically typhus fever, C.F. (typhus) Pos. 1-600 |
| 9956 | R(4) | 16 | — | 36 | C | M | Lymphogranuloma venereum—Frei test—Pos. |

tion and VDRL tests and 1 was reactive only in the Kolmer complement fixation test. The blood that was anticomplementary with the TPCF was also anticomplementary in the Kolmer test.

Table 7 shows results of tests on 5 presumably nonsyphilitic patients who gave nonreactive TPCF and reactive STS tests. These individuals were tentatively classified by their physicians as chronic BFP reactors as none gave history or clinical evidence of syphilis.

A brief abstract of case histories on these patients is as follows:

Patient 1 (Serum No. 7649)—C. L., a 47 year old, white woman was admitted to hospital in 1952, with diagnosis of pneumonia. During hospitalization there was no evidence of syphilitic infection by history or physical examination. The Kolmer, Kline and Kahn tests were reactive. Table 8 gives results of STS performed on this

TABLE 7
RESULTS OF STS AND TPCF TESTS
CLINICALLY NEGATIVE INDIVIDUALS
WITH PERSISTENT POSITIVE STS
BIOLOGICALLY FALSE POSITIVE REACTIONS

| Serum Number | STS Kolmer | STS VDRL Titer | TPCF | Clinical Diagnosis Age | Color | Sex | |
|---|---|---|---|---|---|---|---|
| 7649 | R(3) | 3 | — | 47 | W | F | No history or CES |
| 9887 | R(4) | 4 | — | 51 | C | M | " |
| 9678 | R(4) | 4 | — | 32 | C | M | " |
| 9904 | R(2) | WR | — | 61 | C | M | " |
| 9974 | R(4) | — | — | 35 | W | M | " |

TABLE 8
RESULTS OF STS AND TPCF TESTS ON
SERUM NO. 7649

| Date | STS Kolmer CF | STS Kahn Titer | STS Kline | Date | STS Kolmer CF | STS VDRL Titer | TPCF |
|---|---|---|---|---|---|---|---|
| 1-4-52[1] | Pos. | 256 | Pos. | 7-13-54 | Pos. | 8 | |
| 2-13-52[2] | Pos. | 128 | | 11-9-54 | Pos. | 16 | |
| 5-3-52 | Pos. | 128 | | 1-30-55 | Pos. | 16 | |
| 10-24-52 | Pos. | 128 | | 12-9-55 | Pos. | 16 | |
| 12-11-52 | Pos. | 64 | | 2-2-56 | Pos. | 3 | — |
| 2-24-53 | Pos. | 64 | | | | | |
| 10-7-53 | Pos. | 64 | | | | | |
| 1-6-54 | Pos. | 32 | | | | | |
| 4-13-54 | Pos. | 64 | | | | | |

1. Test performed at Baton Rouge General Hospital.
2. Test performed at our Lady of the Lake, Baton Rouge.
Other tests performed in Div. of Lab., La. State Dept. of Health.

patient in three different laboratories during the past four years. In spite of two courses of treatment, reagin was consistently detected in the blood serum. The physician sent in specimens of blood sera on February 1, 1956, requesting a TPI test as he was convinced that sera from this patient gave BFP reactions. As noted in the table, all STS were reactive but TPCF was nonreactive.

Patient 2 (9887)—B. M., a 51 year old, colored woman, gave a positive STS during routine examination at a New Orleans hospital in 1949, and was referred to the VD clinic for treatment. Patient denied history or previous treatment and showed no clinical evidence of syphilis. STS were reactive, but spinal fluid examination was nonreactive. She returned to clinic in 1953 and twice during 1955 at which time, STS were reactive and spinal fluid nonreactive. On February 1, 1956, the STS were reactive but TPCF nonreactive. Patient was classified as a BFP.

Patient 3 (9678)—A. W., a 32 year old, colored man, applied to Health Clinic for a STS as a prerequisite for course in nursing. The STS were reactive but TPCF was nonreactive. Patient stated that he had been inducted into Army in 1953, and while in service was rejected as blood donor because of reactive STS. Received treatment and discharged from the Army as seronegative. Patient gave no history or clinical evidence of disease.

Patient 4 (9904)—M. J., a 61 year old, colored male, during routine physical examination showed reactive STS. According to available records, patient was suspected of having syphilis on basis of reactive STS on discharge from Army in 1919. Patient showed no clinical evidence or history of syphilis and did not receive treatment. Tests on February 1, 1956, showed reactive STS and nonreactive TPCF.

Patient 5 (9974)—A. S., a 35 year old, white male, during routine physical checkup in January of 1956 showed reactive STS. Patient gave no history or clinical evidence of syphilis. Specimens of blood taken in March showed reactive Kolmer complement fixation test and nonreactive VDRL. A specimen (9974) collected in April showed a reactive reaction with the Kolmer complement fixation test, nonreactive reactions with the VDRL and TPCF. A subsequent repeat test showed similar findings.

Table 9 gives results of TPCF and STS on 12 known syphilitic individuals in varying stages of infection. All of these patients are under treatment. In these few cases, the TPCF appears to be as sensitive as STS in detecting syphilitic infections.

TABLE 9
RESULTS OF STS AND TPCF TESTS
(SYPHILITIC INDIVIDUALS)

| Serum Number | Diagnostic Category | Kolmer CF | VDRL Titer | TPCF | Clinical History Age | Color | Sex |
|---|---|---|---|---|---|---|---|
| 9994 | Primary darkfield (+) | — | — | — | 24 | C | F |
| 4584 | Secondary | R(4) | 8 | R(4) | 26 | W | M |
| 4824 | Secondary | R(4) | 4 | R(4) | 29 | W | M |
| 9640 | Secondary | R(4) | 32 | R(4) | 51 | C | F |
| 9612 | Early latent | R(3) | 2 | R(1) | 32 | C | F |
| 9613 | Early latent | R(4) | — | R(1) | 24 | C | F |
| 9609 | Early latent | — | — | — | 19 | C | F |
| 9608 | Early latent | R(4) | 32 | R(3) | 29 | C | F |
| 9607 | Early latent | — | — | — | 28 | C | F |
| 9611 | Late latent | R(4) | 32 | R(4) | 56 | W | M |
| 9610 | Late latent | R(4) | WR | R(1) | 27 | C | F |
| 9606 | Late latent | R(4) | 16 | R(3) | 31 | C | M |

Preliminary studies on the incidence of the TPCF antibody in sera from 46 individuals showed that the complement fixing antibody was present in 9 of 13 sera from syphilitic individuals which closely correlates the findings of the STS. No TPCF antibody was found with sera from 14 normal individuals or with 15 sera from patients with diseases other than syphilis or with sera from 5 patients whose history and physical examination indicated that their sera gave chronic BFP reactions.

It is evident that the emphasis in the past few years has been focused on the development of test procedures which are capable of differentiating BFP reactions from those in which reaction is due to specific infection with *Treponema pallidum*. Table 10 shows in outline, a summary of our present day concept of the theory of serologic reactions to syphilis, the types of antibodies produced, and the test procedures and types of antigens required to detect them.

By absorption tests, the TPI and TPIA antibodies have been shown to be separate from reagin. TPCF also appears to be separate from reagin. However, TPA test has been shown to detect two antibodies; one of which is reagin. The exact immunological relationship of TPI, TPIA and TPCF to each other has not been determined.

The newer test procedures which are capable of detecting the specific treponemal antibody have proved to be of great help

TABLE 10
THEORY OF SEROLOGIC REACTION TO SYPHILITIC INFECTION

| Antibodies Produced | Test Procedures | Antigens to detect antibodies |
|---|---|---|
| 1. Reagin | APHA Reference | Cardiolipin |
| | Hinton | " |
| | Kline | " |
| | Kolmer | " |
| | Mazzini | " |
| | VDRL | " |
| | Rein-Bossak | " |
| | Kahn | Lipoidal |
| 2. TPI | Treponema Pallidum Immobilization | Live Treponema Pallidum |
| 3. TPIA | Treponema Pallidum immune adherence | Dead Treponema Pallidum |
| 4. TPA | Treponema Pallidum agglutination | Dead Treponema Pallidum |
| 5. TPCF | Treponema Pallidum Complement fixation | Lipid fraction of Treponema Pallidum |

to the clinician in solving certain inadequacies of the STS. However, these test procedures have not yet been evaluated on a sufficiently wide scale basis to determine their efficiency. An evaluation study of all treponemal and cardiolipin tests is being planned for the near future and it is hoped that this will prove as satisfactory as the evaluation study of STS conducted jointly by American Society of Clinical Pathologists and the United States Public Health Service.

Present indications are that the treponemal tests will not replace the STS but will be used in conjunction with them. Moreover, the identification of the chronic BFP phenomenon with other disease entities may lead to use of reagin tests for diagnosis of diseases other than syphilis.

Preliminary studies of the TPCF test in our laboratory show promising results. These studies will be continued on a larger scale as more antigen becomes available. Facilities and experienced personnel for performance of the Kolmer complement fixation test are already available, so that the addition of the TPCF test would not present a problem. If further study of the test substantiates our preliminary findings, it is our belief that the TPCF test will be a valuable specific test for syphilis, especially in studying BFP reactions and in differentiating them from syphilitic infection.

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## INDUSTRIAL DERMATOSES *

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Since World War II the South has grown industrially more than any other section of our country. We are beginning and will continue to see more and more industrial dermatoses and must be able to recognize them as industrial problems to assist management in conquering these hazards of an increasing industralization of our Southland.

About two-thirds of all occupational diseases are industrial dermatoses. According to the U.S. Public Health Service, more than 1 per cent of employees engaged in various industries suffer sometime during the year with industrial dermatitis. An estimated 500,000 people are affected yearly.[1] A study of the compensation records of several states shows that the average loss of time per year for compensated cases of occupational dermatoses is about ten weeks, and the average compensation paid the employee is about $100, plus medical care. It is, therefore, estimated that the annual loss from occupational dermatoses in the United States is in excess of $100,000,000.[2]

The presence of other cutaneous diseases predisposes to industrial dermatitis. Employers in industry should be advised against employing these individuals for they are more likely to become sensitized to any of a number of offending agents, or suffer exacerbations of their dermatosis. The actual causes of industrial dermatoses are many: primary irritants (non-sensitizers) cause approximately 80 per cent of the cases; sensitizers cause approximately 20 per cent of the cases.[1]

Since industrial dermatoses is such a large field we have selected the four most commonly encountered ones, namely, chrome dermatitis, dermatoses due to rubber, dermatitis due to shoes, and chloracne. The various facts and fallacies observed in these industrial dermatoses are presented to familiarize the practitioner with the types of industrial dermatoses one is likely to encounter in an industrial area.

### CHROME DERMATITIS

Chrome dermatitis comprises approximately 10 per cent of all the cases of industrial dermatitis.[2] The chrome compounds (chromic acid, chromates and bichromates) are exceedingly active chemically, and are powerful skin irritants and corrosives. Chief offenders are the alkaline chromates (potassium, sodium and ammonium bichromates). Ulceration of the nasal septum and of the skin is of frequent occurrence in the manufacture of chromates. In factories where chromates are manufactured perforations of the nasal septum, and chrome ulcers on the hands and arms are exceedingly common. According to the resistance of the individual the chrome compounds produce dermatitis of varying severity, affecting primarily the skin and mucous membranes, and may also cause systemic poisoning if absorbed

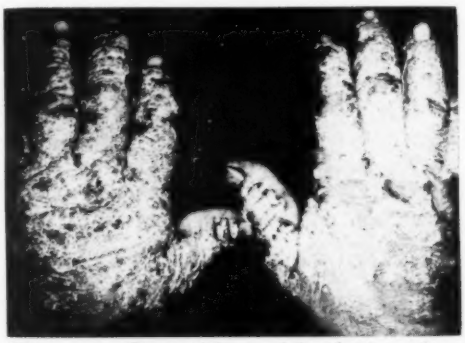

Figure 1. Dermatitis on ink plant worker—possibly due to potassium or sodium chromate used in cleaning the machine.

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through the skin in adequate amounts.[2] The ulcers usually develop when the chrome compounds are deposited on an abrasion.

The extensive uses of chrome compounds in industry are many and varied. They are used in the dye industry, the preparing of alloys, manufacture of inks, chrome tanning, the manufacture of chromium pigments and paints as a mordant, wool dyeing, printing textiles, match making, photography lithography, photoengraving, blue-print developing, chrome plating, synthetic dye manufacture, cement industry, and in the rubber and railroad industries.

Chromium compounds affect the tissue proteins, forming with them chemical compounds, as in the tanning of hides.[6] In strong enough concentrations they corrode the skin and mucous membranes. Strong solutions not concentrated enough to corrode the skin may produce a toxic dermatitis, but in still weaker concentration the chromates may sensitize the skin and cause an allergic dermatitis.[6] As regards frequency, only turpentine, primrose, wood tar and mercury salts are definitely able to cause sensitization oftener. In 1000 cases of occupational dermatitis in the state of Ohio, 60 had chrome ulcers and 31 had chrome dermatitis.[6]

Hall states that sensitivity develops only after a relatively long period of exposure, and once developed, tends to increase rather than decrease in severity. Due to the long period of exposure necessary for sensitization, pre-employment patch testing to reduce the incidence of dermatitis would be worthless.[13]

Chrome Ulcer and Perforated Septum: Chrome ulcers are apparently due to a toxic, necrotizing action of the chromate ion on living tissue, independent of its sensitizing properties. The ulcers are common in the tanning, electroplating, and chromium chemical producing industries. They form when the chemical is introduced into a break in the skin, and are most common on the hands and arms. The ulcers are usually punched out lesions, with raised, indurated borders, and tend to take the shape of the preceding break in the skin. Minimal inflammation is present, and the ulcers are usually painless, healing with depressed atrophic scars as a rule.

Perforation of the nasal septum occurs only in shops in which there are mists or dusts containing chromate. A painless ulcer appears on the cartilaginous portion of the nasal septum, and in several weeks a perforation may occur. The lesion is usually asymptomatic.

Malignant degeneration is not known to occur in either chrome ulcers or perforations of the septum.

Chrome Dermatitis: The incidence of chrome dermatitis is not known, but is thought to be between 1 and 10 per thousand per year, the incidence varying with the type of exposure and the turnover of employees.[18]

Only the hexavalent chromate ion is a sensitizer; metallic chromium or the trivalent compounds are not sensitizing substances.[18] Chromate dermatitis varies from an acute, vesicular weeping eruption, to dry, erythematous, slightly elevated squamous plaques. The most common sites of occurrence are the dorsum of the hands, wrists, and forearms. Chromate dermatitis differs usually from ordinary contact dermatitis in its patch distribution and longer course.

As regards cement dermatitis, it was formerly thought that the dermatitis was due to primary irritation due to the alkaline, abrasive, and hygroscopic properties of cement. It is now thought that dermatitis in cement finishers, fabricators and masons may be due to a specifically acquired hypersensitivity to water-soluble chromate compounds in cement.[5, 16, 17] American cements contain 0.00004 to 0.002 per cent water soluble potassium chromate. Water soluble chromium represents only a small portion of the total chromium in the original cement powder, and hexavalent chromium accounts for over one-half of the water soluble chromium.[5] It is well known that moistened cement may exert a primary irritant action on skin, but various authors[5, 17] have shown that allergic chromate hypersensitivity may initiate and maintain cement dermatitis, as

evidenced by positive patch testing to hexavalent chromium. Soluble hexavalent chromium is apparently present in all cements to a varying degree.

It is also stated that cement artisans are exposed to higher hexavalent chromium levels than is indicated by analysis of cement washings, for as moisture evaporates from cement slurries in contact with the skin, the percentage of hexavalent chromium rises.[5]

The railroad industry is faced with a serious problem in regard to chromate dermatitis. Prior to the advent of the Diesel type of locomotive there was only an occasional case of occupational dermatitis encountered among workers in railroad machine shops. Schwartz [11] stated that the principal dermatologic hazards in the railroad machine shops that he investigated were petroleum and chlorinated hydrocarbon solvents and alkalis, but the use of Diesel locomotives had added Diesel fuel oil, Diesel crankcase oil and coolants containing chromates to the skin hazards.

Sodium bichromate, an autioxidant used in Diesel locomotive radiator fluid, is the most common offending agent.[3] The Diesel locomotive radiator fluid in question is prepared from a powder with the following formula: 66 per cent sodium bichromate, 24 per cent soda ash, 5 per cent disodium phosphate, and 5 per cent sodium silicate.[3] It is used in diesel railroad locomotives and in some stationary units to prevent corrosion in the cooling system. The powder is dissolved in water in an open pail, producing a solution of about 6 per cent sodium bichromate. When this concentrated solution is poured into the radiator of the locomotive, and the radiator is filled with water to its capacity of approximately 210 gallons, a final concentration in the radiator fluid of about 0.08 per cent bichromate solution is produced.

It is difficult to fill and drain the radiator without contaminatng the adjacent parts of the locomotive and splashing the solution on those handling it. Any leakage in the cooling system pump, radiator, or engine jacket will soil the floor and other parts of the locomotive. The employees who prepare and transfer the concentrated power and solutions usually receive the heaviest exposure to the chromate compounds but anyone engaged in cleaning or repairing the locomotive, motors, or the shop area, is exposed to lesser concentrations.

The following measures are suggested as aids in reducing the hazard of contact with the chromatic salts in railroad workers.[3] "(1) The recommended mechanical protective devices—such as rubber gloves, rubber boots, waterproof aprons and sleeves, and protective creams—should be used by those handling chromate compounds in the dry state or the various solutions. They should be particularly careful to avoid spilling this material, thereby contaminating the locomotives and the general shop area with the chromate compound. (2) Those persons working on diesel locomotives who have been found sensitive to chromate should immediately be transferred to other work so that further contact with the substance can be entirely eliminated. (3) Leaks in the radiator system should be repaired promptly by those properly protected, and the contaminated areas thoroughly washed. All parts of the radiator and motor exposed to the chemical should be thoroughly washed to remove any remaining chromate before these parts are transferred into the shop area. (4) Some substance without such sensitizing properties should, if possible, be substituted for the sodium-bichromate solution in the radiator fluid. Failing this, the equipment should be redesigned to effect a minimal amount of spilling of the solution both in filling and in draining the diesel locomotive radiators."

As regards treatment of chrome dermatitis, in its stages varying from the acute eczematous eruption to the chronic stage, there is no specific treatment. Treatment is primarily symptomatic, depending on the acuteness and chronicity. Guy [4] states that the unusual feature of chromate dermatitis is its chronicity and recalcitrance to treatment.

The best approach is prophylaxis, which consists of the folowing measures:

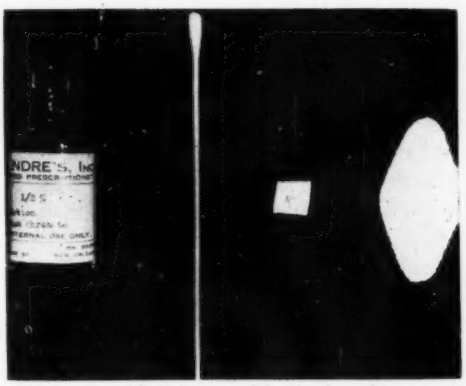

Figure 2. Material used in performing a patch test—

a—Material to be tested diluted to its proper test strength.

b—Cotton applicators used to dampen the skin and the small square of gauze.

c—An elastoplast with a central ring of cellophane (the cellophane does not show in the photograph) which prevents evaporation of the test material.

1. Wearing of long rubber gloves.
2. Use of protective ointments.
3. The use of 5 per cent sodium bisulphite solution for cleansing the hands. This solution reduces the chromium of bichromates with a valence of 6 to that with a valence of 3, the compounds which are less injurious to the skin.

DERMATOSES IN THE RUBBER INDUSTRY

The rubber industry is confronted by relatively few cases of dermatoses. Sensitivity rarely occurs due to crude dry rubber or synethetics,[7] the dermatoses being produced usually by the various complex chemical additives which are ingredients of rubber compounds. Through patch testing it has been proven that antioxidants added to rubber for the purpose of improving its aging properties is the most common cause of leucoderma due to rubber compounds.[23] There are a number of additives which must be added to produce a rubber product. Sulphur must be added to produce vulcanization; accelerators are used as catalysists to speed the vulcanization process; activators are added as a trigger for the accelerator; antioxidants are used to slow the aging of rubber; foaming agents are added to make foam rubber.[7] Synthetic rubber requires the same compounding and additives as latex and crude rubber.

Contact dermatitis due to rubber is more common among workers in industry than among users of finished products, because the workers are confronted with many before vulcanization. Most of the compounds are non-irritating after vulcanization, or "curing", has taken place.

Figure 3. Contact dermatitis due to rubber. (This patient was a file clerk who wore rubber finger stalls.)

"The vulcanization of rubber comprises a chemical reaction by which the physical properties are changed to increase its strength and elasticity and to improve its resistance to changes in temperature." [19] Numerous synthetic organic substances are added to the crude compound to promote vulcanization and/or retard atmospheric oxidation or the effects of oxidation, these compounds being referred to as accelerators, activators and antioxidants. Among the more commonly used accelerators are piperidinium cyclopentamethylene dithiocarbarnate; hexamethylene-tetramine; various members of the carbon disulfide class, especially the carbon disulfide aliphatic amine products; the various guanidines, especially diphenyl-guanidine; and mercaptobenzothiazole and its derivatives.

Activators are compounds which activate acceleration of the vulcanization of rubber. The metallic oxides, especially zinc oxide, are the most commonly used compounds in this group.

Antioxidants are substances which when added to rubber in small proportions retard atmospheric oxidation or the effects

of oxidation. Of the various antioxidants, compounds using the trade name "agerite" produce dermatoses most frequently. "Agerite" hipar and "agerite" powder contain phenyl-B-naphthaylamine, which is a powerful skin irritant.[19] "Albasan" contains

Figure 4. Leukoderma due to rubber.

sufficient B-naphthol to cause irritation of skin, kidneys and eyes.

Of the accelerators, hexamethylenetetramine is the most potent skin sensitizer.

Numerous other accelerators, activators and antioxidants are listed by the National Safety Council as "toxic or irritant."[19]

Plasticizers are frequently added to synthetic resins to increase their flexibility and extensibility. Most of the plasticizers are compounds with a high boiling point, usually above 200 degrees C.[20] "For this reason industrial exposure to the vapors of these compounds is observed only near the areas of vaporization." Mallette and Von Haam[20] studied the effects of 25 commonly used plasticizers in industry. They found that 17 of these compounds proved to be slight or moderate skin irritants; 3 proved to be severe skin irritants; and 5 proved to be moderate sensitizers. Five plasticizers showed no irritating or sensitizing effect.

Various finished rubber products have been known to produce sensitivity, some of the more common being listed below:[22] rubber sponges used for application of cosmetics, rubber gloves (one of the most obvious and best known examples of rubber sensitivity) condomes, rubber bands, rubber dental plates, kneeling pads, rubber panties, eyelash curlers, rubber headrests, rubber bathing cap, rubber dental dams, and rubber in predominantly nonrubber garments, such as elastic on shoes, shorts and hair nets; garters, girdles, brassieres and dress shields. Any of these articles may produce leucoderma.[22]

With the elimination of the additives which are commonly known to produce sensitivity, fewer cases of dermatoses in the rubber industry are seen. Agerite alba (monobenzyl ether of hydroquinone), formerly a widely used antioxidant and very common sensitizer, is now used only by small companies making a single product. The commonest group of dermatoses which are encountered in the rubber industry are eczematizations of the hands, wrists and forearms.[7, 2] The lesions may become secondarily infected, producing generalized infectious eczematoid dermatitis.

With the more modernly equipped factories, safety devices and knowledge of safety recommendations have reduced dermatoses in the rubber industry to a less imposing hazard. Rubber companies have made great strides in eliminating irritating substances, or, where this is not possible, protected the worker from these compounds.

### DERMATITIS DUE TO SHOES

It is interesting to note that definite change in the impression of the causative factor involved in dermatitis venanata due to shoes, as so clearly summarized by Shatin and Reisch in their recent article.[9] Previously, numerous parts of shoes have been incriminated, including the various shoe dyes used, especially aniline; shoe leather; the various substances used in the tanning, finishing and dyeing of leather; various resins, fillers, plastics and rubber adhesives. Gaul and Underwood,[22] and Blank and Miller[23] have emphasized more recently the importance of rubber adhesives in shoes as the causative factor in a great number of cases of shoe leather dermatitis. Shatin and Reisch[9] emphasized that most of their large series of cases of contact dermatitis due to shoes were examples of allergic contact dermatitis due to rubber, and that antioxidants and accelerators are actually the sensitizers in rubber,

as noted by numerous authors.[2, 7, 19-21]

At the Veterans Administration Hospital in Bronx, N. Y., for the five-year period 1947-1951, 1 out of every 10 patients hospitalized because of a dermatologic condition of the feet was diagnosed as contact dermatitis due to shoes.[9]

Most observers have noted a very definite and characteristic clinical picture in the majority of cases of shoe dermatitis, the dermatitis usually being of the anterodorsal portion of the foot. The dermatitis is characterized initially as a mild erythema, gradually progressing to an acute eczematoid process, and may produce autosensitization, involving other parts of the body. Usually, there is an intense pruritis. To the untrained eye the picture may resemble a dermatophytosis; also the two conditions may coexist. Patch tests to various parts of the shoes are very confusing, there being no definite pattern of sensitivity, and also, a certain number of patients have negative reactions to patch tests, even though there is no clinical doubt that the patient has a dermatitis due to sensitivity to materials present in the shoes.[9]

Figure 5. Dermatitis venenata due to shoe lining (rubber).

Usually the appearance of the dermatitis, exacerbations coinciding with the wearing of shoes, and remissions apparently induced by removing the shoes establishes the diagnosis. There may be no history of the purchase of new shoes, and also there may be no correlation between the length of time the shoes are worn and the appearance of the dermatitis. In some cases the dermatitis can appear weeks or months after the purchase of new shoes. Usually the clinical picture is characteristic, both as to the site of onset and its evolution.

Rubber cements are found in various parts of shoes, and rubber is always present in the mid-sole.[9, 21-23] Shatin and Reisch state that these agents are rarely the cause of the dermatitis as compared with the thermoplastic box toe present in most shoes. These authors found that there was a high incidence of their patients (18 out of 31) with shoe leather dermatitis in which the causative agent could be traced to the thermoplastic box toe, "when the dermatitis originates or is localized on the back of the toes," and that these were examples of allergic contact dermatitis due to rubber.[9] The authors state that these patients are easily cured by the use of shoes with a flannel box toe. They routinely test their patients suspected of having a contact dermatitis due to shoes with thermoplastic material and a group of rubbers, and if any of these are positive, the thermoplastic box toe must be eliminated, both as a causative and prophylactic measure, and either the rubber midsole or heel pad if the starting point of the dermatitis appears to incriminate either of these. If the reactions to these stock solutions are negative, the authors find it necessary to investigate the patient's own shoes; they state that this procedure is more difficult and less productive of results.

It has been shown that shoes worn by a large number of patients with foot eruptions are usually moisture repellant.[24] "Shoes that keep environmental water out also keep in psychic and thermal sweat. The foot portion of socks and hose should be made of absorbent fibers, readily permitting the transference away from the feet of psychic and thermal sweat. Shoe

materials should allow the rapid passage of water vapor so that evaporation from the feet can play its important role in the regulation of foot and body temperature".[24]

Variation in the amount of pedal sweat, shoes becoming wet in rain and snow, variable rate of wear of different parts of shoes because of the anatomical structure of the foot, frequent changing of shoes, and individual sensitivity all help explain why one patient develops a dermatitis of the dorsum of the feet, another on the soles, and a third on the heels.

### CHLORACNE

Chloracne is a condition produced by chlorinated hydrocarbons, more commonly, the chlornaphthalenes, chlordiphenyls and chlordiphenyloxides. Acneform cysts and comedones may be formed on the face, back of the ears, shoulders, abdomen, about the navel, groin and genitalia, and may be seen in persons engaged in the manufacture of chemicals for insulating wires, in electricians using flameproof wires, and machinists, oil field workers, oil refiners and paraffin pressmen exposed to oils containing chlorinated hydrocarbons.

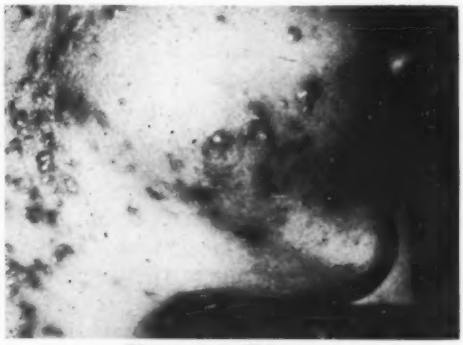

Figure 6. Chloracne.

The lesions occur when the chemicals become lodged in the pores of the skin, plugging the openings and causing retention of the secretions of the glands; the oils also produce stimulation of the formation of keratin; as this action continues comedones and cysts are formed.

The largest number of workers with chloracne are those exposed to the insoluble cutting oils. These oils are used on most machine tools, and basically are composed mostly of refined petroleum oil, with high amounts of sulphur and chlorine added. Chlorinated hydrocarbons are either formed in the oil or are added to it. When these oils are used on heavy cutting or gear grinding operations a mist of oil is seen around the machines and falls on the workers. Chloracne lesions form anywhere on the body where the oil soaked clothing touches the skin. These type of cutting oils are used primarily for their lubricating capacity, aiding the tools in the cutting operation in machine shops.

The soluble oils cause chloracne less frequently. These oils are used primarily as cooling agents, and only secondarily for their lubricating qualities.

Figure 7. Dermatitis due to cutting oils.

Chloracne from synthetic waxes produces lesions with the same characteristics as those due to chlorinated cutting oils. The principal synthetic waxes produced in the U.S. are the chlornaphthalene and the chlordiphenyl containing compounds. They are used as electric insulators on condensors and wires, and in transformers, paints, varnishes and lacquers.

The following measures of prevention of chloracne among these workers are advised by Schwartz:[2]

1. The manufacture of the chlorinated hydrocarbons and the coating of wires and condensers with insulating materials containing the chlorinated hydrocarbons should be done in totally enclosed processes so that the fumes of the insulating substances and of the solvents, if any are used, do not come in contact with the workers.

2. Workers should be provided with

clean coveralls and underclothes daily. These should be laundered at the plant and cleaned in such a way that no chlorinated hydrocarbons remain on them.

3. Shower baths after work should be compulsory. Suitable cleansers should be provided to efficiently remove the insulators from the skin. Sulphonated castor oil is good for this purpose.

4. These measures should apply also to electricians and others who work with wire and condensers insulated with the chlorinated hydrocarbons.

5. Impervious sleeves and aprons should be provided.

Chlorine gas itself and inorganic compounds of chlorine do not cause acne lesions. Naphthalene, diphenyl, benzol or phenol do not cause chloracne unless combined with chlorine, although these solvents can injure the skin by direct contact and can cause systemic poisoning when absorbed.

The treatment of chloracne in general consists of expression of comedones, evacuation of abscesses and cysts, and the frequent use of skin cleansers. X-ray should be used only in special cases.

## COMMENT AND CONCLUSIONS

Those without dermatologic experience are inclined to consider any dermatologic disability as quite minor in comparison with internal disease or loss of limb. This undoubtedly has contributed to the relative lack of consideration given even the disabling dermatoses.

Most skin patients are not very ill, yet their prolonged disability may lead to intense boredom. It is for this reason that a proper attitude is essential to maintain the patient's original high morale. He tends to worry about his slow recovery, the persistent pruritus, his own inactivity, his dwindling bank account, and finally he becomes fearful that he may never again be able to compete equally with his fellow workers.

Future needs for managing dermatoligic rehabilitation more successfully must include expert dermatologic care, a physically sound and protected worker, a modern and clean physical plant, a close liaison between the employer, employee, and physician, an enlightened management, more adequate inspection of industrial hazards, more extensive compensation and rehabilitation measures, and sounder and more complete insurance protection. Every effort should be directed toward the provision of means for relieving the patient of worry about his future security.[27]

We have described only a few of the industrial problems that are beginning to appear in the South as we become more industrialized. No doubt we will see more and more industrial dermatoses. We should be able to recognize these cases as such and to separate them from other dermatoses that simulate industrial diseases of the skin. The physician should visit the plant and examine at first hand the conditions under which the employees work. Only in this way can he do the best possible job to assist the worker and the employer in correcting the problems of industrial dermatoses.

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## HEMATURIA *

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Hematuria is defined as the discharge of bloody urine. Blood may be microscopic in quantity, or the urine may be grossly bloody. It may be bright red blood or it may be dark in color. It may be associated with pain or it may be painless. Hematuria is not a disease but is a symptom of an abnormality of the human body. The bleeding may arise primarily from the genitourinary apparatus or it may arise from some condition or organ removed from the genitourinary apparatus. Since hematuria is a symptom and not a disease, it behoves us as clinicians to delve deeply enough into the case to determine the cause and source of the bleeding so that we may better our patient's chance of being cured. Some of the most serious conditions encountered in the practice of medicine will give the presenting symptom of hematuria and the hematuria may be transitory, thus giving the patient, and sometimes the physician, a feeling of false security concerning the welfare of the patient.

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### ETIOLOGY

Hematuria may be secondary to a systemic disease such as scarlet fever. Most cases of acute nephritis are thought to be secondary to some acute infection such as an acute upper respiratory disease. Within recent years we are appreciating more the fact that allergies to foods, drugs, and contacts cause upsets in the urinary apparatus, and among the symptoms present may be hematuria.

Hematuria may arise from the kidney and be caused by such things as pyelonephritis, polycystic kidney disease, calculi, tumors, hydronephrosis, nephroptosis or tuberculosis. When a complete search is made and no cause is found for renal bleeding that case is then sometimes classified as essential hematuria. Renal hematuria may result from trauma, such as a kidney contusion which might be so mild as to cause microscopic hematuria of short duration, whereas the trauma may be so severe that the kidney may be ruptured causing gross hematuria and severe shock, or even death.

The ureters are not free of the stigma of the source of hematuria, the most likely causes being calculi, tumors, tuberculosis and trauma. The possibility of acute appendicitis must be thought of with pain and hematuria arising from the right side of the abdomen.

Hematuria arising from the bladder may result from an acute cystitis with the typical terminal hematuria associated with tenesmus or straining, or may be painless, gross hematuria resulting from a tumor of the bladder. Stones in the bladder, as well as interstitial cystitis, tuberculous cystitis or some type of allergy can give bladder bleeding. Trauma, such as fractures of the bony pelvis, may produce injury to the bladder and cause hematuria.

The prostate gland, such as a severe acute prostatitis, or an obstruction caused by hyperplasia or carcinoma of the prostate gland can give hematuria.

### DIAGNOSIS AND TREATMENT

The crux of the practice of medicine is predicated on a complete history and physical examination and if the clinician is not

detective enough to make a correct diagnosis, he then should resort to laboratory procedures or consultation. No physical examination is complete without having the urine examined for specific gravity, and the presence or absence of sugar, albumin, red blood cells and pus cells. The last one-half of the voided urine in the male should be used for such an examination whereas all females, regardless of age, should be catheterized to obtain a specimen of urine for examination. It is physically impossible for a female to void an uncontaminated specimen of urine.

Hematuria caused by systemic diseases can usually be determined after a history and physical examination have been made, an example being a youngster who has recently been sick with tonsillitis or some other type infection, followed by swelling of the body and voiding a murky, bloody urine associated with albuminuria. This is your case of Bright's disease, and should be treated as such. Sometimes the sequelae of an infectious process will give the patient chills and fever, pain over the renal area and the presence of pus and blood in the urine. Such are the findings one would expect in a case of acute pyelonephritis. This case should be treated with the appropriate urinary antiseptic until the urine is sterile.

One has to resort to cystoscopy and pyelograms in properly diagnosing hematuria caused by hydronephrosis, nephroptosis or polycystic kidney disease. Hydronephrosis is thought to be caused by obstruction which may be extrinsic in nature, such as an aberrant blood vessel close to the uretero-pelvic junction or adhesions in that region. The obstruction may be intrinsic, such as a stricture of the ureter at the uretero-pelvic junction, thus interferring with the flow of urine from the renal pelvis into the ureter. Many of these kidneys can be saved by an operation in which the obstruction is removed before too much permanent renal damage has been done due to back pressure changes. A nephrectomy should be performed in a kidney which has too much permanent damage, if the opposite kidney is in good condition.

Calculi of the urinary tract is one of our oldest known diseases and is certainly one of the most interesting phases of urology. Joly's book on stones reads like a novel and is filled with knowledge concerning the perplexing problem of calculi. It is a historical fact that some of the mummies found in the excavations of the ancient tombs of Egypt show that renal calculi were present in that area. It is also a historical fact that there were professionals who toured Europe in the twelfth to the fourteenth centuries who "cut for stones". These early surgeons were barbers by trade and operated by a perineal route to remove bladder stones. Stones are more prevalent in certain races and also in certain parts of the world. C. H. Voss has related some of his experience of removing large bladder calculi from children while working as a Medical Missionary in China. We know that the Negro race has but little trouble with urinary calculi. There are many theories propounded regarding the cause of urinary calculi but no one theory proves correct regarding this perplexing problem. Arthur Butt has done some interesting work with hyaluronidase in the prevention of certain types of stones and the late literature mentions the benefit of salicylates in the prevention of stone formation. The whole story is interesting and we look to the future with hope in the handling of stone cases.

A typical case of renal or ureteral colic is the sudden onset of severe pain in the region of the kidney or along the course of the ureter radiating towards the external genitalia. The patient is "on the move" with stone colic; whereas if the pain is from a ruptured abdominal organ the patient lies quietly in flexion trying to splint the peritoneum with the abdominal muscles. Both will give nausea and vomiting and a leucocytosis. The stone colic will often give hematuria, usually microscopic in character. We must resort to pyelography to help in the diagnosis of renal and ureteral calculi. Usually one can palliate temporarily in the case of a small stone not producing urinary obstruction; and at times if the small stone is in the lower one-

third of the ureter it might be extracted with cystoscopic manipulation of catheters. Large stones must be removed surgically and should be done when the urinary apparatus has been completely evaluated. Many nephrectomies could be prevented in stone cases if the diagnosis were made early. Most large bladder stones are secondary to vesical neck obstruction and these cases are usually associated with a marked degree of pyuria and some hematuria. The urinary stream may cut off suddenly when the large stone engages in the urethral opening. Diagnosis is made by cystoscopic visualization and proper x-ray study. The treatment is to surgically remove the vesical neck obstruction as well as the stones. In some cases the choice approach is transurethrally, whereas in other cases the choice approach is open surgery by the suprapubic route.

The triad of symptoms of pain, swelling and hematuria are the cardinal symptoms of tumors of the upper urinary tract. When one considers that the vast majority of these tumors are malignant and that any two of the symptoms of pain, swelling and hematuria usually are found after metastasis has occurred, the seriousness of this condition cannot be stressed too strongly.

Wilms's tumor, found in the first decade of life, is a highly malignant tumor, grows very rapidly and is about 95 per cent fatal within one year after the diagnosis is made. Often the mother notices swelling in the flank while bathing the child, but pyelograms will show a filling defect in the renal pelvis caused by encroachment of the growth into the pelvis which growth also causes hematuria. The treatment is x-ray therapy in order to reduce the growth, followed by nephrectomy, and following the surgery the maximum dosage of x-ray therapy.

About 80 per cent of all cortical tumors of the kidney are hypernephromata which is an adenocarcinoma, and they usually occur more often in men between 45 and 65 years of age. It is an encapsulated growth but when the growth breaks through the wall of the pelvis it will produce hematuria and again the pyelogram will have a filling defect in the pelvis of the kidney. These tumors are resistant to x-ray therapy. The treatment is nephrectomy.

Papillary tumors of the renal pelvis or the ureter will give hematuria and also a filling defect on pyelographic study. The treatment is nephrectomy and ureterectomy, the ureterectomy being necessary because of the fact that the papillomatous growth has a tendency to seed itself down the ureter and into the bladder.

Acute cystitis is a very common urinary complaint, occurring most commonly in the female. Some of the typical symptoms are urinary frequency, nocturia, urgency, burning, tenesmus and often hematuria. The hematuria usually occurs at the end of the urinary act and is called terminal hematuria. These cases have no fever. Catheterized urinalysis will reveal red blood cells but will also present pus cells and organisms. The treatment is symptomatic care plus the proper urinary antiseptic. The treatment should be continued until the urine is sterile.

Unfortunately, hematuria from the bladder does not end with cystitis, stones, trauma and interstitial cystitis. When one considers that the cardinal symptom of bladder tumors is painless, gross hematuria in two-thirds of such cases, and when one considers that all bladder tumors are malignant or potentially malignant, and that the hematuria stops in three-fourths of the cases within one to three days whether or not treatment is given, it is reasonable to presume how inadequate treatment of such a case is until a diagnosis is made. Do not give pink pills or blue tablets and ask the patient to return if the hematuria persists. The diagnosis is made by careful cystoscopic visualization of the bladder. Caulk described bladder papillomata as epithelial in origin, projectile in character, invasive in nature, indolent in progress, with the disposition to be situated upon the bladder mucous membrane. These tumors may be multiple but three-fourths are located close to the trigone of the bladder.

The urologist can usually classify the degree of malignancy present by the cystoscopic appearance of the tumor. Using Broders' classification of 1922, the Grade I tumor with less than 25 per cent malignant cells, cystoscopically will be a papilloma attached to the bladder mucous membranes by means of a long, thin pedicle. The Grade II tumor with 25 to 50 per cent malignant cells will have a thick pedicle, whereas the Grades III and IV will have no pedicle but will arise gradually from the deeper layers of the bladder.

In 1946, Jewett and Strong established the present therapeutic and prognostic criteria by correlation of clinical and pathological findings, namely, that there is a definite relationship between the depth of the tumor invasion of the bladder wall to the therapy and prognosis. They found that cancer of the bladder which had invaded deeply into the muscularis was usually fatal to the patient regardless of the type of treatment used. One cannot cure the surgically incurable cancer of the bladder. Reports indicate, however, that more than 50 per cent of cases are cured by any of the accepted methods of treatment if the cancer has penetrated to less than midway through the muscularis.

Three per cent of all deaths in the United States caused by malignant diseases is caused by cancer of the bladder. The disease is twice as prevalent in men as in women.

The most conservative way to treat bladder tumors is to be radical. Strike fast and with all the force and resource you have at your disposal. The low grade type of tumor can usually be controlled by heroic transurethral resection and fulguration of the tumor mass. Never discharge bladder tumor cases for bladder tumors are prone to recur, often in another part of the bladder. By cystoscopic examination every few months the recurring tumors can be destroyed by transurethral fulguration and resection while the tumors are small. To procrastinate with bladder tumors is sometimes fatal to the patient.

In more advanced bladder tumor cases a suprapubic cystostomy with severe fulguration of the tumor masses and a segmental resection of the bladder is often the treatment of choice. Cystectomy and a diversion of the urinary stream is sometimes done. Vincent Vermooten of Dallas reports favorably on the use of radioactive cobalt in the treatment of cancer of the bladder. This procedure holds much promise for cancer of the bladder.

No attempt has been made to cover the entire field of hematuria, the thought being to review briefly some of the urologic conditions encountered in which hematuria plays a part. If we can remember that some of our very serious conditions can cause hematuria, especially the painless, gross hematuria found in cancer of the bladder, then the effort put forth in the writing of this paper will have been well rewarded.

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## ATYPICAL AND MINOR EPILEPTIC SEIZURES *

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NEW ORLEANS

Physicians, and most laymen, have no difficulty recognizing a generalized or *grand mal* epileptic seizure. In fact, the diagnosis is usually made by doctors who never actually witness the attacks but accept the accounts of the patient, his relatives and friends when they describe the sudden snuffing out of consciousness, the fall to the ground, vigorous tonic and clonic movements, biting of the tongue, involuntary urination or defecation and the post-seizure confusion, stupor and headache. If

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more confirmation is needed, the burns, scars or bruises sustained during the attack may be noted during the physical examination. Also, certain neurologic signs, often present for several minutes or even hours after a seizure (such as the Babinski sign) may be observed.

Patients who complain of bizarre alterations of consciousness, which may be brief or prolonged but are decidedly less dramatic than a generalized epileptic seizure, pose different diagnositic problems. If the patient has *grand mal* seizures in addition to these minor, atypical or partial episodes, the physician usually grasps the relationship. However, if a patient has only minor seizures, their epileptic nature may not be promptly appreciated. The term "epileptic equivalents" has been used in the past for such phenomena although clinicians since Hughlings-Jackson [1] have realized that these attacks are epileptic, just as the generalized convulsion is, and the term "equivalent" has no significance. Several important concepts have emerged since Jackson's early clinical expositions and these deserve emphasis. First, the pattern of the minor, atypical or partial seizure is dependent on the anatomic structures in the brain that are involved by excessive, abnormal electrical activity. In other words, the peculiar behavior, hallucinations, autonomic symptoms, bizarre memories and motor activity and other manifestations form this striking clinical picture because specific areas of the brain are the site of origin and limited spread of the epileptic discharge. Second, these seizures, like generalized fits, may be either idiopathic or symptomatic. In the former instance no cause can be specified, even after a careful diagnostic survey, whereas in the latter any one of diverse etiologic factors may be important, such as brain tumors, head injuries, meningitis, encephalitis, birth trauma, cerebrovascular disease, toxic metabolic disorders, and degenerative diseases of the brain. This second point obliges the physician to take a complete history, perform a thorough physical examination and conduct appropriate laboratory studies to establish or exclude etiologic possibilities. Third, these minor seizures have important clinical, electroencephalographic and therapeutic distinctions from the *petit mal* seizures of childhood and focal cortical seizures of the Jacksonian type. Various names, all with some merit but none of them completely satisfactory, have been given to the minor epileptic attacks that are clearly not *grand mal, petit mal* or Jacksonian. These include psychomotor epilepsy [2,3] and temporal lobe epilepsy [4,5], to name only two of the most popular. The clinical manifestations are so polymorphous and the structures possibly involved so complex (temporal lobe, insula, rhinencephalon, diencephalon) that descriptive or anatomic terminology is too cumbersome and laborious for routine clinical use. Among clinicians particularly interested in the disorder, clinical, anatomic and electroencephalographic observations are often utilized in nomenclature but for most clinicians recognition of these seizures and their varied etiologies is enough, and the term, minor epileptic seizures, is probably adequate.

Several summaries of cases will illustrate the range of possibilities.

### CASE REPORTS

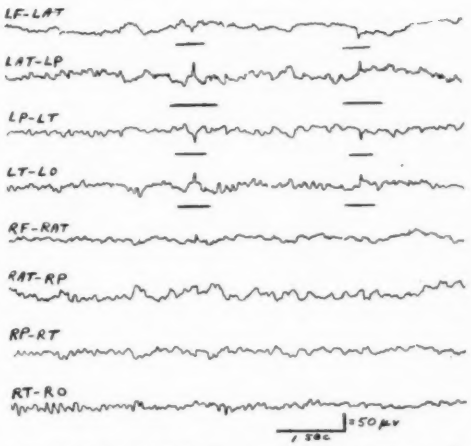
*Case No. 1*: F. E. T., a man 20 years old, had had measles encephalitis characterized by delirium, stupor and several generalized convulsions at 7 years of age. After recovery from the acute encephalopathy, he had had recurrent attacks, as often as ten a day or as few as one every three months, during which he would become suddenly frightened for no particular reason, then feel chills sweep down his back and increase in crescendo fashion until his entire body was cold. He would become intensely nauseated, immoble and slightly confused although not amnesic. His stomach "growled" and he belched and passed flatus frequently. The attack would terminate in about three minutes and would be followed by a severe headache in the right frontotemporal area. Neurologic examination and an electroencephalogram showed no abnormalities. He tolerated 0.1 Gm. of mebaral three times a day with no side effects. The seizures, which were briefer and associated with much less severe autonomic manifestations, occurred only one to three times a month during the following seven months.

There are several points of interest about this case. An obvious etiologic fac-

tor, measles encephalitis, had produced cerebral damage that resulted in an unusual pattern of seizures with impressive autonomic reactions and mild confusion. Measles encephalitis has been mentioned as one of many infectious or postinfectious causes of what Gastaut [6] called diencephalic psychomotor epilepsy. That the diencephalon, particularly the hypothalamus, is involved in these seizures seems apparent from the clinical description. Isolated fear as an aura or initial manifestation in epilepsy has been frequently observed.[7] The normal electroencephalogram in this patient, made in a period between seizures, is not unusual for Gastaut [6] indicated that this may be the case or there may be interictal electroencephalographic findings. Gibbs and Gibbs [2] described 14 and 6 per second spikes in sleep in some similar cases, which they call thalamic and hypothalamic epilepsy.

*Case No. 2*: D. C., a school girl aged 17 years, suddenly began having "spells" at the age of 15 years. She had approximately one seizure every two days. The attacks were characterized by a strange, unrecognized taste followed by "blacking out" and amnesia for the next several seconds. She would not fall but seemed confused, made faint muttering noises and tugged at nearby objects or aimlessly crumpled paper. The entire episode would last only several seconds to a minute, after which the patient would resume her preseizure activity. She had never had any *grand mal* seizures. The only significant fact in the history was that her birth was preceded by prolonged, difficult labor. Results of neurologic examination and laboratory studies were within normal limits. An electroencephalogram showed random spikes in the left anterior temporal, left temporal areas (Figure 1). Treatment with 0.1 Gm. of dilantin and 0.064 Gm. of mebaral three times a day has resulted in freedom from seizures for twenty-two months.

The gustatory aura, amnesia, confusion and coordinated, repetitive but purposeless movements are distinctive and form one of the easily recognized types of minor seizure referred to as psychomotor epilepsy or temporal lobe seizures. Temporal area spike discharges in the electroencephalogram are commonly associated with these seizures, most often in sleep,[2] although this relationship is not an invariable one.




(L—left, R—right, F—frontal, C—Central, P—parietal, O—occipital, T—temporal and AT—anterior temporal.)

Fig. 1: (Case 2). Electroencephalogram showing left anterior temporal, left temporal random spike.

*Case No. 3*: W. N. E., a contractor 31 years old, had had approximately one episode of amnesia every month for seven months. On one occasion, he left home at 10:30 a.m. feeling well and was found seven and one-half hours later, asleep at his summer camp many miles from the city; he did not recall anything that had happened in the interim. His family physician, who saw the patient during two of the seven episodes, described him as apprehensive with hesitant, somewhat slurred speech "as though he were drunk." Both alcoholism and psychopathy had been excluded, however, by many years of observation of this patient by his family physician. About fifteen years before the onset of these amnesic attacks, while playing football, the patient had sustained a head injury followed by periods of loss of consciousness and amnesia. Complete study of the patient including an electroencephalogram made while he was awake and asleep revealed no abnormalities. A second electroencephalogram made six months after the first showed anterior temporal, temporal random spikes (Figure 2). Treatment with 0.1 Gm. of dilantin three times a day and 0.25 Gm. of mysoline twice a day has resulted in freedom from seizures for the past eight months.

Amnesia always poses a difficult diagnostic problem in that the physician must first decide whether it is due to epilepsy, hysteria or head injury, or whether it is feigned, as in psychopathic persons.[3] Careful history is the most valuable aid. The neurologic examination may or may not be

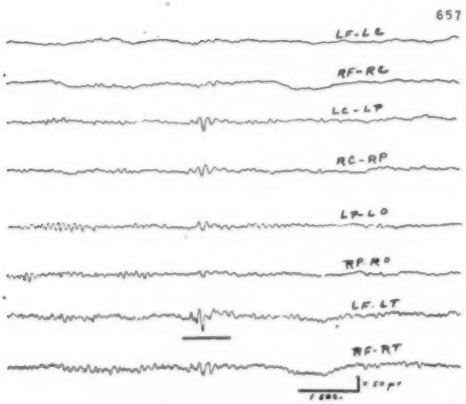



Fig. 2: (Case 3). Electroencephalogram showing diphasic spike from left temporal area.

helpful. Definite electroencephalographic findings may confirm, but not prove, certain clinical suspicions. And finally time and observation will usually furnish a definitive answer.

*Case No. 4*: J. F. C., a farmer 44 years old, began having episodes which he described as "double-thinking" in October 1955. He would suddenly become slightly confused and hear people talking to him, but he could see that those around him were not speaking at all. He was aware that the voices he heard were hallucinations. On another occasion while walking in the forest he had heard a popular song. This was so vivid that he looked around for a phonograph, even though he recognized this as an auditory hallucination. These hallucinations were so disturbing that he did not discuss them with anyone for fear they would consider him psychotic, until intermittent attacks of aphasia and a *grand mal* convulsion made him seek medical advice. At first results of all studies were within normal limits, including an electroencephalogram. But equivocal pneumoencephalographic observations, increasing attacks of aphasia and a second electroencephalogram, which showed a left temporal slow wave focus (Figure 3), led to arteriography, craniotomy and discovery of a glioblastoma multiforme in the left temporal lobe.

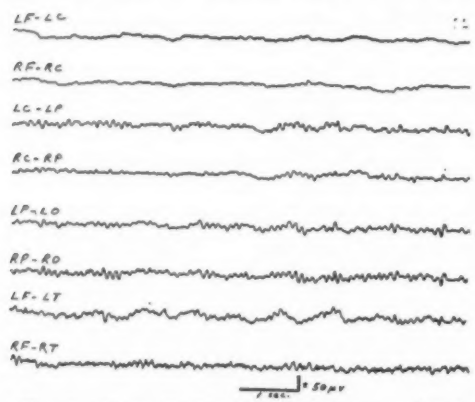



Fig. 3: (Case 4). Electroencephalogram showing intermittent slow wave focus in left temporal area.

*Case No. 5*: C. M. T., a male student 21 years old, had had four seizures in six weeks. The patient would suddenly experience burning pain in the right side of the neck which extended upward, behind the ear to the vertex of the scalp. He would then sit or lie down and remain motionless. This was followed by confusion and giddiness (not true vertigo) and then amnesia for several seconds. When his memory returned, his vision would be blurred for a few seconds and a diffuse headache would develop and last several minutes or hours. Past and family histories, and neurologic examination revealed no abnormalities. The electroencephalogram showed much normal activity but paroxysmal slowing and increase in voltage of the rhythms in the central areas were noted occasionally; during hyperventilation there was a large build-up or diffuse slowing and increase in voltage (Figure 4). The patient has been taking 0.25 Gm. of mysoline twice a day for seven months and has had no seizures.

Burning pain is not a frequent initial symptom in epilepsy, although Whitty [8] reported 5 cases in which burning pain similar to that in causalgia was an epileptic aura. The brief alteration in consciousness, amnesic component and abnormal electroencephalographic findings make the epileptic character of these spells apparent, although the total clinical picture really gives no clues to the cerebral areas involved or the site of origin of the discharge, unless one accepts Whitty's hypothesis that an aura of burning pain suggests involvement of the parietal cortex.

## DISCUSSION

The cases presented were selected from a routine office and hospital neurologic practice and represent no truly unique problems. Patients with similar histories also visit general practitioners and specialists. The cases described were selected for presentation because they bring out several points considered earlier. These minor, atypical or partial seizures are epileptic phenomena. If the patient also has *grand mal* seizures and a family history of epilepsy, this fact is easier to appreciate.

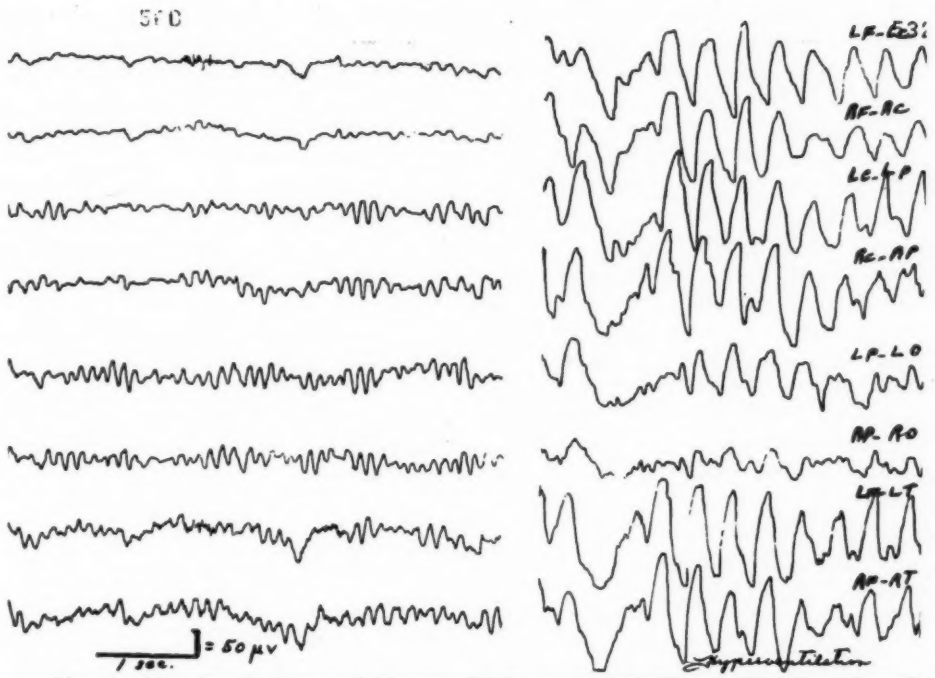



Fig. 4: (Case 5). Electroencephalogram showing normal rhythms on the left, and on the right, large build-up (slowing and increase in voltage) during hyperventilation.

However, some patients have only minor attacks and in some the manifestations are so atypical and bizarre as to suggest other diagnoses, such as faints or syncope, apoplexy or strokes, hysteria or schizophrenia. Faints and fits are frequently confused because of the common factor of loss of consciousness, but the stereotyped sequence of events in a faint, the occurrence in the erect posture or after sudden emotional shock, the gradual onset with pallor, weakness and visual blurring are too familiar to require much comment. Additional factors, such as postural hypotension, carotid sinus sensitivity and heart block, will be apparent in certain cases. Minor seizures have no such order and their very disorderliness should arouse suspicion of epilepsy, though it is true that there are some similarities, and a central nervous system that is unstable for the maintenance of consciousness is common to both.[9] Cerebrovascular accidents are readily excluded from the differential diagnosis because there are no neurologic residuals between attacks and often these minor seizures occur much too frequently to be considered even remotely as cerebrovascular accidents. It should be mentioned that minor and major seizures are occasionally residuals of cerebrovascular accidents such as thrombosis, hemorrhages, or embolism. Hysteria and schizophrenia are often eliminated after careful history and observation make it clear that the seizures occur in sudden, paroxysmal fashion and the patient is normal or nearly so between attacks, whereas in patients with psychiatric disorders this is not usually the case. Here again it should be pointed out that patients with epilepsy may also have personality disorders and emotional disturbances, so that neat distinctions are not always possible. The neurologic, general physical and electroencephalographic examinations are all helpful adjuncts but an accurate medical history is the most important item and a diagnosis of epilepsy cannot be made on laboratory studies alone, including the electroencephalogram.[10]

If the physician thinks that a given patient with minor or atypical seizures has epilepsy, some thought should be given to distinguishing *grand mal*, *petit mal* and Jacksonian types from the type of seizures under consideration. This can be done by clinical analysis of the seizure patterns. This also gives clues to the areas of brain involved (temporal lobe, insula, diencephalon, rhinencephalon). With tentative localization, various etiologic factors should be considered in the light of the past medical history, age of onset and the results of a complete study of the patient. In 2 of the 5 illustrative cases herein presented no obvious cause of the seizures could be determined. In the other 3, one had had measles encephalomyelitis, one a malignant brain tumor, and one an old head injury.

Treatment depends on the cause. In patients with focal lesions, such as tumors or vascular malformations, palliative or curative neurosurgical therapy is of great importance. Some investigators [11] have resected portions of the temporal lobe of patients with psychomotor epilepsy without demonstrable neoplasms but in whom medical therapy had not controlled the seizures. The initial enthusiasm for this approach has been tempered somewhat during the past few years and it is still too early to evaluate results. Each case must be weighed on its individual merits before surgical treatment is decided upon or rejected. Medical therapy is based on use of anticonvulsant drugs and general measures such as prohibition of alcohol, counseling and supportive psychotherapy. Not everyone is agreed on the most efficacious drugs and it is difficult to conduct adequate statistical surveys. Everyone does agree that these minor, atypical, psychomotor or temporal lobe seizures are the most difficult types of epilepsy to treat. We have found dilantin, mebaral, mysoline and mesantoin useful either alone or in various combinations. The first three have less side effects than mesantoin and should be tried first.

## SUMMARY

Certain brief alterations in consciousness, unusual episodic behavior, and peculiar sensations, thoughts, and hallucinations may be manifestations of epilepsy. The patient may or may not have had generalized epileptic seizures at some time, and there may or may not be a history of epilepsy in the family. Causes of these attacks are varied and not always clearly determined, but in certain cases can be traced to injury, infectious diseases, and, in a few cases, tumors of the brain. By careful history, examination, and some laboratory tests the physician distinguishes these minor epileptic seizures from true faints, non-neurologic disease and psychiatric disturbances. Once their nature is understood, various methods of treatment, depending on the cause, are available.

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## DISCUSSION

Dr. Gregory S. Ferriss * (New Orleans): Dr. Moossy has given us a very excellent summary of the problem of minor epileptic seizures. His cases illustrate several varieties of epileptic patterns, and they are of diverse etiologies.

In practice, minor seizures unaccompanied by major seizures present very difficult problems in diagnosis. The medical history, with emphasis on delineation of a constant pattern with sudden or paroxysmal onset, is usually the most valuable part of the clinical work-up. The frequency of occurrence of personality disturbances, often of a hysterical or a schizoid type, has been noted many times. History-taking is often difficult, the epi-

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leptic phenomena being hidden within a mass of other symptoms. It is in such cases, as well as in cases in which no witness is available to describe the seizures, that the electroencephalogram may become very helpful. The electroencephalographer has somehow erroneously come to be thought of by many people not usually concerned with epilepsy as the final arbiter of its diagnosis. This is not so. However, the EEG frequently does show inter-seizure abnormalities of a type known to occur in epileptics, and furthermore, "activation" techniques, especially intravenous metrazol, have been developed to show such abnormalities when they are not seen in the usual record. Metrazol can also be given to precipitate a clinical seizure of the patient's type, should such doubts be remaining that observation of a seizure were deemed essential to diagnosis.

We should all be aware of the pitfalls of the premature use of anticonvulsants as a "therapeutic trial" in attempting to establish the epileptic nature of suspected minor or atypical seizures, though later a good response may ultimately be gratifying confirmation. As Dr. Moossy emphasized, the treatment depends on the cause, and since, in almost all cases, these seizures are symptomatic of cerebral pathology, every effort should be made to obtain an exact and specific etiologic diagnosis in every case. Often the indicated workup is extensive, but the temptation to treat the symptom (the seizure) alone could lead us to miss the occasional potentially curable lesion, such as vascular lues, meningioma, etc.

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## USE OF RADIOACTIVE IODINE FOR INTRACTABLE ANGINA PECTORIS *

ALLAN M. GOLDMAN, M. D. †
NEW ORLEANS

In the treatment of refractory heart disease it is necessary to review the therapy and consider both extrinsic and intrinsic factors that increase cardiac work. For increased efficiency, careful use should be made of digitalis, vasodilator drugs, low salt diet, and diuretics. Sedatives should be employed to stabilize emotion, and exercise must be restricted to conform with the functional capacity of the heart.[32]

Evaluation of thyroid function is indicated because an overactive thyroid is known to create a greater burden on the cardiovascular system. With exacerbation of a toxic goiter, evidences of angina pectoris and congestive heart failure become more severe;[9] whereas operative removal of such a goiter is followed by dramatic relief of angina and heart failure.

Induction of a hypothyroid state in a euthyroid patient, previously reported by many authors, represents an extension of this therapeutic principle. Purposeful induction of myxedema lessens the demands on the heart of a seriously ill patient by reducing its work and requiring a lower level of oxygen consumption.[7] This is especially true where arteriosclerotic coronary vessels and previous myocardial infarction impair the circulation to the cardiac muscle with resultant anoxemia and angina.

Good results with this method have been reported by Blumgart and associates[12] as early as 1933. Improvement was noted in over 350 patients with angina pectoris and congestive heart failure when myxedema was induced by total thyroidectomy. However, the hazards of operation in an already chronically ill patient are readily recognized. Other surgical measures advocated include sympathectomy, posterior rhizotomy, pericardial injury, omentopexy, pericoronary neurectomy, and arterialization of the coronary sinus.[8] Further work is necessary to determine the value of these and other procedures now under investigation.

Following the work of Astwood[2] with the thiourea drugs in hyperthyroidism, medical thyroidectomy has been attempted. Thiouracil and propythiouracil have been utilized in euthyroid patients with angina pectoris in order to obtain the necessary hypometabolism.[4, 13, 19, 20, 28, 31] Unfortunately, only some of the patients responded, and an indefinite period of administration was required to maintain the hypothyroid state. Serious drug reactions have been reported, including agranulocytosis and death in a few instances.[3, 14, 22, 24, 25, 26, 27]

Following the successful use of radioactive iodine, $I^{131}$ in hyperthyroidism, its use was suggested in euthyroid cardiac

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patients. The thyroid has a remarkable affinity for iodine and appears to be the only organ capable of concentrating that element to a high degree.[33] Unlike the action of roentgen-ray, that of $I^{131}$ is selective. Since $I^{131}$ emits both beta and gamma rays, safety precautions must be observed. A completely equipped laboratory is necessary for proper handling of the material, with apparatus for measuring by remote control and for dilution. Sensitive measuring equipment and trained personnel are essential to guard against the danger of excretion and external radiation. Accurate measurement of urinary $I$,[131, 18] and direct uptake over the gland[16] have previously been described.

Before therapy with $I^{131}$ can be instituted, a tracer dose must be given to determine the uptake of the gland. In patients whose uptake is unduly low because of prior ingestion of iodine, or who have recently had intravenous pyelography or cholecystography, Blumgart[7] recommends deiodination of the thyroid by means of the thiourea derivatives. After a suitable time, tracer studies may be instituted and a therapeutic dose of $I^{131}$ may be administered.

Freedberg and co-workers[17] reported the pathologic effects of $I^{131}$ on the normal thyroid gland of man, describing postmortem material in 16 euthyroid patients who died at varying intervals after $I^{131}$ therapy. Seven days after oral administration of 20 millicuries, no histologic changes were noted that could be attributed to $I$.[131] Fourteen and twenty-four days after administration of 59 and 26.4 millicuries, respectively, massive radiation effects were detectable. Distortion and destruction of the normal thyroid architecture were noted to be maximal at the center of the gland. Edema and degeneration of the stroma, acute vasculitis, with thrombosis and hemorrhage, epithelial swelling and vacuolization, follicular destruction, and polymorphonuclear infiltration were all present. The periphery of the gland revealed less damage, but the follicles were disrupted, and colloid and round cell infiltration were evident.

Further changes in patients who survived a longer period included increased fibrous stroma, lymphocytic infiltration, and arteriolar intimal thickening and hyalinization. The follicular epithelium became desquamated and admixed with a fragmented or globular colloid. Also noted were atypical cells with large hyperchromatic nuclei. The thyroid gland was largely replaced by dense fibrous tissue in patients who survived for three hundred and sixteen to one thousand and sixty-nine days after treatment with $I$.[131] The remaining follicles were extremely disrupted. No irradiation damage to the parathyroid glands, pituitary glands, trachea, larynx, or adrenal glands was reported. No thyroid neoplasm and no toxic effect on the kidney, peripheral blood, or blood-forming organs that could be directly related to $I^{131}$ have been reported in the literature.[8]

### CLINICAL INDICATIONS AND CONTRAINDICATIONS TO $I^{131}$ THERAPY

In selecting patients for $I^{131}$ therapy, Freedberg and associates[15] called attention to the fact that the course of angina is often irregular and characterized by periods of unexpected exacerbation and remission. When all standard forms of treatment have failed and the patient shows evidence of continued incapacity in spite of extreme restriction of activity, radioactive iodine therapy should be considered. Jaffe and associates[21] recommend a careful history, physical examination, roentgenogram of the chest, electrocardiogram, complete blood studies, urinalysis, determination of basal metabolic rate, protein bound iodine, blood cholesterol, and radioactive iodine tracer studies prior to therapy. They treated 100 euthyroid patients by the multiple small dose technic, using 6 millicuries of $I^{131}$ in 20 cc. of water orally each week for five weeks. Radiation thyroiditis and the liberation of large amounts of thyroxin into the blood stream were avoided. Gradual rather than sudden myxedema was produced. When additional doses were necessary, a period of two months was allowed to elapse, since $I^{131}$ has a physical half-life of eight days.

Most authors[7-10, 33] agree that favorable

candidates for $I^{131}$ therapy include the following: (1) patients with severe angina, who respond poorly to careful medical treatment, (2) patients in whom sufficient time has elapsed to make spontaneous improvement unlikely, (3) cooperative, alert, intelligent, and emotionally stable patients who are willing to refrain from excessive use of tobacco and to remain on a low fat diet, (4) patients with such severe angina as to be frequently awakened at night, making adequate rest impossible and thus preventing them from earning a living, (5) patients with frequent attacks on slight to moderate exertion, such as walking short distances or climbing a flight of stairs or following meals, (6) patients with no signs of hypothyroid states, i. e., basal metabolic rate and iodine tracer studies within normal range and blood cholesterol not abnormally high, (7) patients with no serious concomitant disease who have been relieved of some or all cardiac pain after suffering one or more myocardial infarcts, but whose economic status and occupation will permit them to refrain from strenuous physical work.

Contraindications to $I^{131}$ therapy include: (1) emotionally unstable individuals particularly subject to depressive episodes, (2) intermittent claudication in the legs, (3) patients with rheumatic arthritis or active rheumatic fever, (4) tendency toward embolic phenomena that may dominate the clinical picture at any time, (5) rapidly progressive clinical course (malignant hypertension, syphilitic heart disease), (6) low initial BMR (less than minus 15 per cent), (7) acute myocardial infarction, (8) poor risks for follow-up treatment and careful future management.

### SELECTION OF PATIENTS

The present series includes 13 patients treated with therapeutic doses of $I^{131}$ and followed from 1951 to the present time. Patients were selected on an individual basis when all other forms of therapy failed to produce improvement. Seven of the patients were women and six were men, their ages ranging from forty-five to seventy-nine years. A tracer dose of 50 microcuries was used, and the uptake was measured at a distance of 17 cm. directly over the gland in the Biophysics Department at Touro Infirmary. Normal uptake of radioactive iodine is considered to be between 10 and 40 percent of the tracer dose in twenty-four hours. Although some of the patients were outside this range, all were considered to be suitable candidates for this therapy. One patient with an uptake of 50 per cent was not considered to be clinically hyperthyroid. Treatment doses varied between 25 and 40 millicuries. In the 13 patients in the present series, a single large therapeutic dose was used because it was desired to shorten the period of irradiation and secure an earlier onset of hypothyroidism and because the early supply of the radioactive element from the Oak Ridge Laboratory was uncertain. This single dose resulted in postirradiation thyroiditis, release of large amounts of thyroid hormone, and exacerbation of the patients' symptoms. Since this course has proved unwise, future patients will be treated by divided doses. Later experience reported by Blumgart and associates[8] in 1,070 euthyroid patients from many clinics has proved the value of divided doses given at weekly intervals until the desired therapeutic result is obtained.

Twelve of the patients were hospitalized to secure maximal improvement prior to irradiation therapy and to reduce postirradiation hazard. One received $I^{131}$ as an outpatient but had to be hospitalized later because of increasing severity of his angina following postirradiation thyroiditis. In all patients some therapeutic result was obtained within four weeks to four months. Results are summarized in Table 1. Five of the patients died, 3 from acute myocardial infarction, 1 following the development of acute pulmonary edema, and 1 from a cerebrovascular accident. A lymphoblastic lymphoma developed in one patient nine months after administration of the treatment dose. It is interesting that this patient has several sisters and brothers with malignant disease. Follow-up studies of the 8 surviving patients now varies from two to five years. Whenever possible, recent basal metabolic rates, as

TABLE 1
RESULTS OF TREATMENT OF ANGINA PECTORIS WITH $I^{131}$

| Pt. No. | Diagnosis | % Uptake $I^{113}$ * | Treatment $I^{131}$ (mc) | Results of Therapy |
|---|---|---|---|---|
| 1 | HCVD<br>ASHD | 50.7 | 40 | Striking improvement 1 month after treatment. |
| 2 | HCVD<br>Myoc. Infarct. | 24.2 | 35 | Moderate improvement in 5 weeks; striking improvement in 2 months. |
| 3 | HCVD<br>Diabetes<br>ASHD | 19.9 | 25 | Slight improvement in 4 weeks; striking improvement in 3 months. Died suddenly 4 months after treatment following acute myocardial infarction. |
| 4 | ASHD<br>Myocardial Infarction | 34.6 | 40 | Moderate improvement in 2½ months. Lymphoblastic lymphoma in neck biopsy 10 months after treatment. |
| 5 | HCVD<br>ASHD | 26.4 | 35 | Acute myocardial infarction 2 weeks after treatment. Moderate improvement in 3 months, striking improvement in 5 months. |
| 6 | HCVD<br>Myoc. Infarct. | 20.0 | 35 | Moderate improvement in 2 months. Generalized hypertrophic arthritis. |
| 7 | HCVD<br>Myoc. Infarct. | 29.9 | 25 | Slight improvement in 6 weeks; striking improvement in 5 months. Died 16 months after treatment following cerebrovascular accident. |
| 8 | HCVD<br>Myoc. Infarct. | 34.6 | 40 | Died 7 weeks after treatment following 2nd. myocardial infarction. Insufficient time for improvement. |
| 9 | HCVD<br>Myoc. Infarct. | 15.5 | 40 | Moderate improvement 4 months after treatment. Mild cardiac failure in 5th month. |
| 10 | HCVD<br>CHF | 36.0 | 35 | Died 5 months after treatment following acute pulmonary edema. |
| 11 | ASHD<br>Myoc. Infarct. | 41.2 | 40 | Striking improvement in 2½ months. One episode of mild failure following pneumonia. |
| 12 | HCVD<br>Myoc. Infarct. | 32.5 | 25 | Striking improvement in 2 months. |
| 13 | HCVD<br>CHF | 9.06 | 40 | Died in 3 weeks of acute myocardial infarction. Insufficient time for improvement. |

* Distance 17 cm. in all cases except Nos. 3 and 12, in both of which distances used were 10 cm. and 30 cm.

well as blood cholesterol studies, have been carried out. The latter are high in most instances and correlate well with the clinical hypothyroid state. Results were classified as excellent in 5 cases, good in 1, and fair in 2 cases. (Table 2)

There are few objective tests to determine the presence or absence of angina pectoris. The patient's statement about chest pain was correlated with information obtained about his physical activities and mental attitude.[33] In each instance, onset of clinical improvement coincided with the appearance of the symptoms and signs of mild myxedema.[8] Fullness and puffiness of the face, swelling of the eyelids, fatigue, hoarseness, dryness of the skin, and increased sensitivity to cold were noted early. Later symptoms included swelling of the tongue, stiffness and pain in the joints, and the sensation of a swollen abdomen. The time when hypometabolism and clinical improvement will occur cannot be predicted by the physician or patient. With relief of anginal pain and onset of myxedema, a daily dose of 6 to 12 mg. of desiccated thyroid should be administered. In each patient, thyroid dosage must be adjusted to

TABLE 2
FOLLOW-UP RESULTS OF TREATMENT OF ANGINA PECTORIS WITH $I^{131}$

| Pt. No. | Interval From Treatment to Improvement | Result of last BMR | Blood Cholesterol and Esters | | Present Clinical Symptoms | Follow Up Exam. Duration | Result |
|---|---|---|---|---|---|---|---|
| 1 | 5 weeks | —32% | | | Occasional angina, limited activity. | 30 mos. | Fair |
| 2 | 5 weeks | —24% | C<br>CE | 420<br>350 | No. pain. Complete relief returned to nursing 28 months later. | 19 mos. | Excellent |
| 3 | | | | | Patient died. | 4 mos. | |
| 4 | 10 weeks | —32% | C<br>CE | 980<br>790 | Almost complete relief but complicated by lymphoma. | 20 mos. | Excellent |
| 5 | 14 weeks | —22% | C<br>CE | 570<br>390 | Rare anginal pain, normal activity. | 27 mos. | Excellent |
| 6 | 8 weeks | | | | Rare cardiac pain, mild failure well controlled. | 32 mos. | Good |
| 7 | | | | | Patient died. | 16 mos. | |
| 8 | | | | | Patient died. | 7 wks. | |
| 9 | 18 weeks | —14% | C<br>CE | 395<br>330 | Only occasional angina. Mild symptoms cardiac failure. | 30½ mos. | Fair |
| 10 | | | | | Patient died. | 5 mos. | |
| 11 | 10 weeks | —38% | C<br>CE | 320<br>170 | Rare pain. Able to attend court without pain. | 26 mos. | Excellent |
| 12 | 8 weeks | —15% | C<br>CE | 465<br>450 | Rare use nitroglycerine, normal activity. | 5 yrs. | Excellent |
| 13 | | | | | Patient died. | 3 wks. | |

maintain the lowest metabolic level at which maximal relief from cardiac disease may be experienced with minimal discomfort from myxedema. Occasionally, this may not be possible. Most patients are maintained at a BMR level of minus 20 to minus 25 per cent on a daily dose of 6 to 30 mg. of thyroid extract. According to Blumgart,[8] an occasional patient may experience recurrence of symptoms, because the residual thyroid tissue has regenerated and caused the metabolic rate to approach pretreatment level. In such a case, thyroid medication should be withdrawn, and after administration of a tracer dose, an additional therapeutic dose may be given.

Kurland and associates[23] described radiographic and electrocardiographic changes in cardiac patients who were euthyroid prior to induction of persistent hypothyroidism by one or more doses of $I.^{131}$ The duration of the hypometabolism ranged from two to fifty-three months, with an average of twenty-seven months. Changes in size and configuration of the heart were studied in 27 patients, and variations in the electrocardiograms were examined in 28 patients. Ten of 13 patients with good or striking improvement in angina pectoris from $I^{131}$ treatment showed no increase in cardiac size. In 2 others the cardiac size remained unchanged during periods of twenty-six and thirty-eight months of relief, respectively, but later increased during exacerbations of angina pectoris and congestive heart failure. Cardiac enlargement progressively increased in 5 of 6 patients with angina pectoris unimproved by $I^{131}$ treatment, whereas 6 patients with chronic cardiac insufficiency showed no

cardiac enlargement during most of the nineteen to fifty-three months of hypometabolism. Two patients with both angina pectoris and cardiac insufficiency received definite benefit from $I^{131}$ therapy, even though cardiac size progressively increased. The development of myxedema was associated with electrocardiographic changes, which included decrease in voltage, flattening or inversion of the T waves, and slight increase in QT interval. In the present series, several electrocardiographic tracings revealed similar results, but it must be remembered that progression of organic heart disease and the use of certain drugs will modify existing electrocardiographic patterns. Treatment with thyroid extract produced reversion of these changes, with no further progression despite continued hypometabolism. These studies suggest that "myxedema" heart", as characterized by angina pectoris or congestive failure and striking electrocardiographic and radiographic changes does not occur in patients with prolonged, controlled $I^{131}$-induced hypothyroidism.

Cholesterol values obtained following the production of myxedema in the present series and reports of others [6, 8] raise the question of whether or not such patients are predisposed to atherosclerosis. Blumgart and associates [6] reported clinical and postmortem observations in 8 patients who survived from one to thirteen years following total thyroidectomy and in whom hypometabolism with elevated cholesterol values was present. These were younger patients with rheumatic heart disease. None had complete occlusion of the coronary arteries, and only 3 of the 8 had slight narrowing of one of the main stems. In the other 5, arterial damage from atheromatosis and atherosclerosis varied greatly, but conditions were similar to those observed in euthyroid patients. Daily use of small doses of thyroid extract in the latter group might exert some protective action.

## DISCUSSION

Treatment of the euthyroid patient with severe angina pectoris is symptomatic, the rationale being that reduction of total metabolism of the body will reduce the cardiac requirements of these severely ill patients to a level within their cardiac reserve.[32] Each case must be considered individually, although some broad indications for this treatment may be accepted. Rosenfeld [30] stressed the importance of frequent and continued observation of such patients, especially after treatment. Patients with severe cardiac abnormalities are subject to many complications that occur in the course of their disease. Since their state of health is dynamic and changeable rather than static, it must be watched even more carefully after administration of $I,^{131}$ since the effects of mild myxedema and the variable effects of extract of thyroid therapy are added to the previous disease.

The complex relationship of the thyroid with other endocrine glands raises the question of the need for other hormones. Although there is no evidence as yet that the duration of life is prolonged by such treatment, the many comfortable months to years it affords are welcomed by the seriously ill cardiac patient. In the future, a simple surgical procedure may be devised to improve blood supply to the myocardium. Until then, attention must be directed toward means of reducing the load carried by a chronically diseased heart. No untoward sequelae to radiation have been noted thus far, but further studies seem indicated. Varied dosage schedules of $I^{131}$ are being employed by other clinics [6, 8, 21, 30] to clarify the advantages and disadvantages of the different programs of treatment.

## SUMMARY

Thirteen euthyroid patients with intractable angina pectoris have been treated with radioactive iodine after all conventional forms of therapy failed. Persistent hypothyroidism was produced in all patients. Eight of the 13 are living at the present time. A single massive irradiation dose was employed in all instances, and the resultant thyroiditis effected temporary exacerbation of anginal symptoms. Divided dosage is indicated to avoid this hazard. No toxic effect has been noted on the hematopoietic system or the kidneys. Sur-

viving patients are being maintained on minimal doses of thyroid extract to prevent clinical myxedema. Indications and contraindications for $I^{131}$ therapy are reviewed. The favorable results obtained in the surviving patients in this series seem to warrant further careful study of this method of relieving intractable heart disease.

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## DANGEROUS FEATURES IN THE NEW SOCIAL SECURITY AMENDMENTS LAW

The efforts of organized medicine suffered a serious defeat at the hands of the Social Security lobby with the enactment of the bill entitled, Social Security Amendments of 1955 (HR 7225). It was signed on August 1, 1956, by President Eisenhower. This law has certain features which were strenuously opposed by the AMA and by the majority of the constituent state medical associations.

The provision of the bill regarded as most dangerous is that which provides benefits for total disability after age 50. This feature maneuvers physicians into the social insurance part of the Social Security program and would contrive to have the doctors working at first part time, and later, entirely under the direction of some part of this federal agency. Since Louisiana is the state whose government has ventured furthest toward the welfare state, physicians of Louisiana have good reason to regard the law as ominous, and there is a reasonable expectation that it will be the basis for further ventures into the realm of the welfare state. The basis for such a fear is the history of successive amendments to the original Social Security law since 1935, and the parallel observation that forty years ago when the income tax became law no one suggested the extent of its present power. The contention that this sequence of events is threatening is supported by the provisions in the amendments to the Social Security Act. Certain amendments of the 81st, the 82nd, and the 83rd Congresses provided payment from public funds for physicians to treat disabled charity patients covered by the Social Security Act, and then certain other amendments established the "disability freeze" entailing a projected medical certification. The precedent for the determination of disability on terms of a federal program was thus established. These amendments were the preparation for the present and most recently enacted law, which provides these benefits.

These dangers were anticipated and comment was made in these columns * explaining this attempt to enact the state medicine program piece by piece. When the most recent law was being considered in Congress, no hearings were allowed by the House, but the Senate held extensive hearings. The Louisiana State Medical Society sent a representative to appear before the Finance Committee of the United States Senate, which was considering the bill, and

* New Orleans M. & S. J., Editorial, 104:549, (July) 1952.

the undesirable features were explained. The comment was made that age limits would inevitably be lowered by successive amendments. It was stated that the number of those who could qualify for total disability under the loose definition given in the bill would be far greater than 300,000. The reason for making this statement is that each one of those 160,000 practicing physicians knows among his own patients at least 5 to 10 persons who could qualify. When mental cases are included, the number potentially receiving benefits in ten years would be 2 to 3 million.

If such is the case, the operation of this law will soon require an increase in the payroll tax, or substantial support from other tax sources.

From the point of view of the individual, as well as that of the national economy, rehabilitation of the disabled is to be preferred to disability support or maintenance. Competent authorities have estimated that up to 9 out of 10 disabled persons can be rehabilitated if they have the will and opportunity. Payments to the disabled under this law would have the tendency to discourage effort and initiative, retard rehabilitation, and retard return to productive employment. Nearly every doctor knows of patients who claimed and successfully maintained that the effects of injuries prevented their working—until "the case was settled," when they immediately returned to full employment.

The feature of the law that gives physicians the most concern, from a professional point of view, is the determination and care of the disability. There are no exact medical, legal, or social methods of determining total disability that are uniformly applicable. As a result, its determination is often dificult or impossible. Among the majority of those who would seek coverage in this field under this law it would be a matter of the will.

In certifying as to the applicant's status the doctor will be placed between the patient and the government. Except in a few obvious cases he cannot satisfy both. The patient will pursue his project from doctor to doctor. As in the field of insanity, he may be disabled in one state and competent in another. A clamor will arise for an official determination by medical governmental authority. This would likely be followed by the demand that the same official care for the patient while disabled. As the age limits of 18 and 50 approach each other in successive legislative alterations, a full fledged system of gradually expanding state medicine will be developed among us.

When the bill was up for action before the Senate, the final vote was 90 to 0 in its favor. In the vote on the disability provision previous to the final vote it was 47 to 45, the two Senators from our state voting to sustain the disability feature and, in our opinion, voting against the best interests of medicine, and in favor of this distinctly socialistic trend. The decision of the majority was manifest in the face of clear-cut explanations and distinct representations in regard to the contrary point of view. We have in this, and in other recent legislation, the unhappy spectacle of both parties competing with each other for an opportunity to embrace some socialistic principle. To protect the public against such legislation it is not enough to inform the Congress of its dangers. The public has to be brought to the realization of the dangers and then the public may lead the Congress. As a friend of the author said recently, "If every man is to be a King, the supplication of 'God save the King' seems to be the order of the day."

# ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

## DR. GRAVES HONORED

We quote the following from the AMA Secretary's Letter of July 27th:

Some men are content to sit around and wait to go to Heaven while others make Heaven out of their surroundings.

That's what Dr. James Q. Graves has done down in Monroe, Louisiana.

Friends and townspeople in all walks of life honored Jim, who has served 27 consecutive years as a member of the A.M.A. House of Delegates, on the occasion of his 50 years of practice.

It must have been a "heavenly affair" because, judging from the prominent newspaper accounts, the beloved doctor was showered with praise from the lips of many speakers, some of whom were his long-time patients.

Jim was guest of honor at a big testimonial dinner at St. Francis Hospital in Monroe. Dr. R. B. Robins, of Camden, Ark., a former vice president of the A.M.A., and past president of the American Academy of General Practice, was the principal speaker.

Dr. Graves, who developed a happy facility for collecting friends by the score, spoke too. He touched on the medical past and then took a glimpse at the future, predicting among other things that research "will develop vitamins to meet the needs of every organ of the body," and that "gastric and duodenal ulcers will be cured or prevented by the correction of the physiology or the stabilization of the nervous mechanism of the human body."

Jim spiced his speech with many an interesting anecdote taken from his long and benevolent career in medicine.

There was the time, years back, when he set out on horseback to see a patient. He and his horse crossed a river swamp safely on a flatboat, but on the return trip the flatboat sank. His horse swam about two miles before reaching dry land with the young doctor hanging onto his tail.

"He saved my life," Dr. Graves recalled.

Doctor Jim is a man with many friends; he collects them like other people collect rare china, precious gems or cigar wrappers. He has the uncanny knack of finding the friends for his collection everywhere. It may be the man who serves him or the man he serves. It may be a casual acquaintance, a policeman on the corner, or the town banker. Jim must have learned long ago that friendship can be bought with kindness, consideration, thoughtfulness and tolerance. His colleagues in the House of Delegates know that he has all of these qualities . . . and his patients do, too.

One of them, a woman whom he has attended since 1917, recalled that her husband owes his life to Dr. Graves, "Who got up from his bed with fever to come to him during the flu epidemic in January, 1920."

Jim, the son of a cotton planter, is a fine physician who is extremely modest and lives unpretentiously. He and his wife, the niece of a former Supreme Court Justice, were blessed with four daughters—all of whom are now married and have children of their own.

"Sometime during each week, but not all at the same time, they have dinner with us," he said, adding: "That's what makes life worth living."

The Louisiana State Medical Society wishes to concur in the above and add their congratulations on the honor so gratefully conferred on him by loyal confreres and fellow citizens, an honor and recognition unquestionably merited. Jim is one of the most outstanding physicians of the State and deserves any acknowledgment that the people of his State might show him for his wonderful deeds.

Jim has been loyal to his profession and has created with his friends confidence and respect.

Jim has represented our State Society as a delegate to the American Medical Association House of Delegates for many years, with distinction and credit, and is the oldest AMA delegate in line of service, and his fellow delegates respect and love him.

All glory to you Jim, our friend and hero! We salute you!

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## FROM WASHINGTON

The social security bill (H.R. 7225) now is the law of the land—Public Law 880 of the second session, 84th Congress. Increased OASI taxes to support payments to the disabled at age 50 become payable on January 1, 1957. Disability benefits become payable on July 1, 1957. Until and unless new regulations are issued, doctors will follow the same procedure in connection with this new law that they follow under the disability freeze amendment now in effect. The physician makes his medical findings and turns in his report to the state agency in charge, usually the office or department of rehabilitation. The decision then is made by the agency, based on vocational as well as medical findings, as to the applicant's disability.

Following is the complete text of a statement

issued by President Eisenhower August 1 when he announced he had signed the social security bill, H.R. 7225:

"I have today signed H.R. 7225, the Social Security Amendments of 1956. The new law embraces a wide range of changes in old-age and survivors insurance, the public assistance programs, and child welfare services.

"This Administration's strong support of the social security program was demonstrated by the broad expansion and improvements enacted in 1954 at my recommendation. The 1954 Amendments, which extended coverage of the program to millions of additional persons and included higher benefits for all who were then or who would become beneficiaries, have had a major impact in bringing greater security to our people.

"The new law also contains certain major provisions which were recommended by the Administration. It extends social security coverage to about 600,000 additional farm owners or operators and about 225,000 self-employed lawyers, dentists, and others.

"It provides for increased Federal funds to encourage better medical care for the needy aged, blind, disabled, and dependent children. This will help meet a critical problem for these groups.

"Another Administration proposal placed increased emphasis, in public assistance programs, on services to help more needy people build toward independence. The law initiates new programs of grants to train more skilled social workers and to support research in ways of helping people overcome dependency. Another Administration proposal will increase funds for child welfare services.

"The law also includes provisions about which the Administration had serious reservations in their initial form; these provisions were modified and improved before their final enactment and now meet, in part, some of the Administration's objections.

"The original proposal to lower the retirement age for all women was changed to provide that employed women and wives may accept reduced benefits at an earlier age or obtain full benefits at age 65. I am hopeful that this provision will now have no adverse effect on employment opportunities for older women. The law allows full benefit at age 62 for widows because of their special needs.

"Congress also modified somewhat the original proposal to provide disability benefits at age 50 or above. A separate trust fund was established for the disability program in an effort to minimize the effects of the special problems in this field on the other parts of the program—retirement and survivors' protection. We will, of course, endeavor to administer the disability provisions efficiently and effectively, in cooperation with the States. I also pledge increasing emphasis on efforts to help rehabilitate the disabled so that they may return to useful employment.

"The original proposal would have imposed a 25 percent increase in social security taxes on everyone covered by the system. I am pleased that the tax increase has now been cut in half. Our actuaries report that while they cannot estimate costs of the disability program with certainty, the tax increase should be adequate to finance the benefits, assuming effective administration.

"Although there were difference of opinion over separate provisions, the final legislation was approved overwhelmingly by Congress. In signing this legislation, I am hopeful that this new law, on the whole, will advance the economic security of the American people."

Physicians are expected to be called upon soon to help qualify thousands of disabled workers for early social security payments, under a revised program.

The task was assigned to the medical profession in a new Act of Congress H.R. 7225 which allows disabled workers to start collecting social security checks at age 50 instead of 65.

For more than two years the AMA and other medical organizations fought the bill with every weapon at their command. They argued it would be "virtually impossible" for physicians to determine eligibility, and it would be costly to taxpayers, as well as a step toward Federal control of medicine.

### Key Role for MDs

But the Senate overrode their objections and voted 47 to 45 to adopt the disability payments proposal approved earlier by the House.

The new legislation amending the basic social security law is expected to apply to more than 250,000 disabled workers over 50. Physicians are assigned a key role in determining eligibility. Among other things, an applicant for such disability payments must:

1. Prove he is "unable to engage in any substantial gainful activity." "Substantial" is not defined.

2. Have a "medically determinable physical or mental impairment which can be expected to result in death or be of long-continued and indefinite duration."

3. Submit physician reports detailing diagnosis, history and clinical findings to establish the nature, severity and probable duration of the condition.

4. Accept any available state vocational rehabilitation services unless there is good cause for refusal.

5. Have a permanent disability at least six months before collecting any payments.

The legislation leaves it up to the Government to spell out the detailed eligibility procedure.

# MEDICAL NEWS SECTION

## CALENDAR

### PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

| Society | Date | Place |
|---|---|---|
| Calcasieu | Fourth Tuesday every other month | Lake Charles |
| East Baton Rouge | Second Tuesday of every month | Baton Rouge |
| Morehouse | Third Thursday of every month | Bastrop |
| Natchitoches | Second Tuesday of every month | |
| Orleans | Second Monday of every month | New Orleans |
| Ouachita | First Thursday of every month | Monroe |
| Rapides | First Monday of every month | Alexandria |
| Sabine | First Wednesday of every month | |
| Tangipahoa | Second and fourth Thursdays of every month | Independence |
| Second District | Third Thursday of every month | |
| Shreveport | First Tuesday of every month | Shreveport |
| Vernon | First Thursday of every month | |

### SOUTHWEST LOUISIANA GRADUATE MEDICAL ASSEMBLY

The 9th Annual Meeting of the Southwest Louisiana Graduate Medical Assembly will be held in Lake Charles, September 14-15. All physicians are invited to attend this meeting which is approved for Category I by the American Academy of General Practice. Presentations during the scientific sessions will include:

Oxygen Therapy, A. J. Ochsner, M. D., Chief of Anesthesiology at St. Francis Cabrini and Baptist Hospitals, Alexandria, La.

Roentgenology in Obstetrics, William Snow, M. D., Chief Radiologist, V. A. Hospital, Shreveport, La.

Antibiotic Diseases, J. H. Seabury, M. D., Professor of Medicine, L. S. U. School of Medicine, New Orleans, La.

Hazards of Steriod Therapy, Theo C. Panos, M. D., Professor of Pediatrics, University of Texas Medical Branch, Galveston, Texas

Acute Cholecystitis, James D. Rives, M. D., Professor and Head of Dept. of Surgery, L. S. U. School of Medicine, New Orleans, La.

Surgery and the Cardiac, a panel discussion, Drs. A. J. Ochsner, J. D. Rives and T. C. Panos

The Differential Diagnosis of Fever, Theo C. Panos, M. D.

Roentgen Study of the Chest, with Special Reference to Emphysema, Atelectasis and Edema, William Snow, M. D.

Dermatologic Manifestations of some Systemic Diseases, Henry W. Jolly, Jr., M. D., Chief of Division of Dermatology, Our Lady of the Lake Sanitarium, Baton Rouge, La.

Pathological Physiology of Lower Nephron Nephrosis, J. F. A. McManus, M. D.

Rectal Bleeding, James D. Rives, M. D.

Pulmonary Mycoses, J. H. Seabury, M. D.

Differential Diagnosis & Initial Treatment of Cerebro-Vascular Accidents, Earl Rafes, M. D., Attending Neuro-Surgeon at Hotel Dieu and Baptist Hospitals, Beaumont, Texas

Also on the scientific program will be two CPC's and a Curbstone Consultation. Lt. Gov. Lether Frazer will be a guest speaker at the Saturday luncheon. A full range of social activities have been planned for attending physicians and their wives.

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### SOUTHERN MEDICAL ASSOCIATION'S GOLDEN ANNIVERSARY CELEBRATION

This celebration will be held at The Read House in Chattanooga October 2-3, 1956, exactly fifty years from the day, October 2-3, 1906, the Association was organized. This celebration will take place in Chattanooga and at the Read House where, on October 2-3, 1906, representatives from Alabama, Florida, Georgia, Louisiana, Mississippi and Tennessee met for its organization. Our own Dr. Dowling was elected Secretary-Treasurer which position he held for three years.

Louisiana has been honored with the Presidency four times—Dr. Isadore Dyer in 1911, Dr. Oscar Dowling in 1915, Dr. C. E. Bass in 1926 and Dr. Lucian A. LeDoux in 1948.

This celebration in Chattanooga on October 2-3 should not be confused with the Golden Anniversary Annual Meeting to be held in Washington, November 12-15.

Dr. Dwight H. Murray, President of the American Medical Association, will, with other medical celebrities, deliver addresses at the meeting.

This is an auspicious occasion and merits a large attendance from the respective sixteen States and District of Columbia now comprising the Association.

Why not mark your calendar and plan to attend this meeting on October 2-3? A grand program is being planned for your entertainment and enjoyment. Don't fail to meet us in Chattanooga.

## ELASTIC SUIT DEVISED AS HYPOTENSION TREATMENT

The pattern of grandpa's red flannels has been altered slightly and used to make a pressure suit for people with a serious type of low blood pressure.

The tight-fitting suit, made of elastic cotton-rayon knit material, applies pressure over the lower half of the body and helps prevent a patient with orthostatic hypotension from fainting when he stands up. For some it allows a return to work or enables standing for longer periods on the job.

The garment is described in the May 12 Journal of the American Medical Association by Herbert O. Sieker, M. D., John F. Burnum, M. D., John B. Hickam, M. D., and Kenneth E. Penrod, Ph. D., of the departments of medicine and physiology, Duke University School of Medicine, Durham, N. C.

Orthostatic hypotension—sometimes called postural hypotension—results from the inability of peripheral arteries to constrict and maintain enough pressure to force the blood back to the heart. The condition may be associated with diabetes mellitus or may follow a sympathectomy, an operation to relieve excessively high blood pressure. In other cases its cause is unknown. A person with the disorder is all right as long as he is lying down, but when he stands, there is a sudden drop in blood pressure and he becomes faint.

## CONSULTANT SAYS SECOND COUSINS MAY MARRY

A medical consultant recently contradicted the notion that all cousins who marry will have defective children.

In a query to the Journal of the American Medical Association, a physician asked if it would be wise for a girl to marry her second cousin—the grandson of her father's brother.

The unnamed consultant said in the May 12 Journal that it would be all right—if the ancestry on both side for three generations was sound physically, intellectually and emotionally.

The danger to any offspring of a marriage between cousins of sound ancestry would not be much greater than if the parents were unrelated, he said.

## HAZARDS OF HAIR BLEACHING ARE OUTLINED

In becoming a blonde the peroxide way, a woman stands the risk of losing many of the most prized properties of her hair, the secretary of the American Medical Association's committee on cosmetics warned.

Mrs. Veronica Conley said in the May issue of Today's Health, published by the A.M.A., that a woman must answer three questions before bleaching her hair. They are: Will her skin blend well with blonde hair? Can she afford the added professional care? Is her hair sufficiently healthy and sturdy to stand the assault of a bleaching agent without disastrous damage?

Mrs. Conley pointed out that no matter how pretty a particular shade of blonde hair is on one person, it may not be on another. Complexion and hair must complement one another. Treating the hair with peroxide most often produces a harsh yellow shade, particularly unflattering to all but the very young. Adding a hair dye of suitable shade in the blonde range softens and refines the harshness of peroxide, but the strain on the hair is considerably increased when it is subjected to two hair-coloring processes, she said.

## OPEN TREATMENT OF BURNS

The open method of burn therapy has significant advantages, John Calvin Weeter, M. D., believes. He says this method prevents maceration of tissues "with the danger of subsequent infection." Also is open therapy, "the crust actually amounts to a heat-sterilized patch of tanned skin which acts as a protective barrier over the viable tissue beneath." Other advantages are freedom from "cumbersome dressings and freedom of movement."

Dr. Weeter discusses in the **Journal of the Kentucky State Medical Association** (54:155 (Feb.) 1956) his own technic in treating both third and second degree burns with emphasis on the necessity for early debridement and grafting.

In preparation for grafting, he recommends that the open wound be covered with fine mesh gauge impregnated with Furacin Soluble Dressing (Eaton) "because of its inhibiting effect on the common bacterial skin contaminants." In reference to donorsite care, he says that an effective method "is the application of Furacin impregnated fine mesh gauge placed next to the open wound."

Dr. Weeter is from Louisville, Ky.

## POTASSIUM AMINOSALICYLATE

Five out of six tuberculosis patients intolerant to paraaminosalicylic acid (PAS) or its sodium salt are able to take the potassium salt now being marketed by Eli Lilly and Company as Pulvules 'Paskate' (Potassium Aminosalicylate, Lilly).

The new form of this therapy thus enables as high as 94 percent of all tuberculosis patients to take it without the extreme nausea, vomiting, and diarrhea that limit the usefulness of PAS in its other forms.

Clinical tests show that because of its greater solubility 'Paskate' gives higher blood concentrations of PAS than equal doses of sodium PAS. Also, 'Paskate' contains no water or hydration and, hence, provides, gram for gram, 11 percent more PAS for absorption than does NaPAS.

# WOMAN'S AUXILIARY TO THE LOUISIANA STATE MEDICAL SOCIETY

## A MESSAGE FROM THE AUXILIARY CONSULTANT

**Mrs. Arthur A. Herold, Sr.**

I would like to tell you a few facts about your National Auxiliary. I say "Your" advisedly, for it depends upon you as to whether or not your National Organization will be successful with its program. Your National Auxiliary has gained world wide recognition and it is now considered one of the most influential of the various women's organizations. National can only plan programs and projects; it is, however, the State and Parish organizations that must put these into effect.

Our National Auxiliary now has a membership of over 72,000, but the A. M. A. has a membership of well over 122,000. This is a fertile field for those of you who have organizational ability. It is not only important to contact the wives of practicing physicians, but also the wives of residents and interns. We should begin early to indoctrinate these women with the feeling that it is a privilege to belong to our groups. It is a select group, for in order to be eligible for membership, one has to be the wife or widow of a physician. Explain to these prospective members that their husbands, by virtue of their profession, occupy a position in their community unequaled by that of any other group; therefore, the day they become the wives of physicians they came more or less into the lime light, and what they do and say may have pleasant or unpleasant repercussions on the parent organization as well as on their own.

This year, National is stressing the needs of the medical schools. The Special Committee to promote this program is called, as you know, the American Medical Education Foundation. This committee needs you to make the lay public realize how necessary it is to support the medical schools in order to prevent the federal government from assuming the responsibility. The nurse recruitment program is very important and should be enlarged to include occupational therapists, medical technologists, medical social workers and physical therapists. There is an alarming shortage in all of these fields. Of course, there is always the legislative program that needs careful study so that we may be able to correctly interpret it to the general public.

Keep your national organization informed of all your activities; National is interested and eager to know what you are doing. If you do this, you may also help her to pass on to other auxiliaries worthwhile experiences as well as valuable information.

As all of you know, the Auxiliary on all levels is dear to me and please believe me when I say everyone of you is important to the medical auxiliaries; they need you and want you as active members not as idle by-standers.

Note: Mrs. Herold is also Parliamentarian for The Woman's Auxiliary to the American Medical Association.

Mrs. Mildred G. Carter,
Publicity Chairman, Woman's
Auxiliary to the LSMS

Courtesy of: **News and Views**

# BOOK REVIEWS

*Vaginal Hysterectomy, Indications, Technique and Complications;* by Laman A. Gray, M. D., Springfield, Illinois, Charles C Thomas, 1954, Pp. 137, Price $4.75.

The author introduces the book as written for the operator who undertakes vaginal hysterectomy at intervals but does not do so many that he is an expert.

The various sections deal with the history of development of vaginal hysterectomy, indications, preoperative preparation, postoperative care, complications, and a long list of references.

ADOLPH JACOBS, M. D.

*The Practice of Dynamic Psychiatry;* by Jules H. Masserman, M. D., Philadelphia, Pa., W. B. Saunders Co., 1955, Pp. 790, Price $12.00.

This massive book is written in Dr. Masserman's facile, literary style which matches well his goal of expressing in one volume the psychiatric interview, the syndromes of behavior disorder, the clinical aspects of psychiatry vis a vis the jurist, etc., and clinical therapy. He covers a vast number of ancillary and corallary topics copiously illustrated by cases.

This is a text serving primarily the psychiatrist, in training and in practice, but the excellent chapters on the psychiatric examination, techniques of history taking and the mental status examination might be of interest to the general practitioner. It can certainly be recommended as a reference book of high value. The bibliography itself is quite valuable.

IRVIN A. KRAFT, M. D.

## PUBLICATIONS RECEIVED

Paul B. Hoeber, Inc., N. Y.: Diagnosis and Treatment of Peripheral Vascular Disorders, by David I. Abramson, M. D.

Charles C Thomas, Publisher, Springfield, Ill.: Ulcers of the Legs, by P. Piulachs, Chief Professor Surgeon in the Faculty of Medicine of Barcelona, (dedicated to Dr. Rudolph Matas); Natural Childbirth, by H. B. Atlee, M. D.